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(1) Hanson, I. R. and Hingson, R. A., *Current Researches in Anesthesia and Analgesia*, 29:136 (May-June) 1950.

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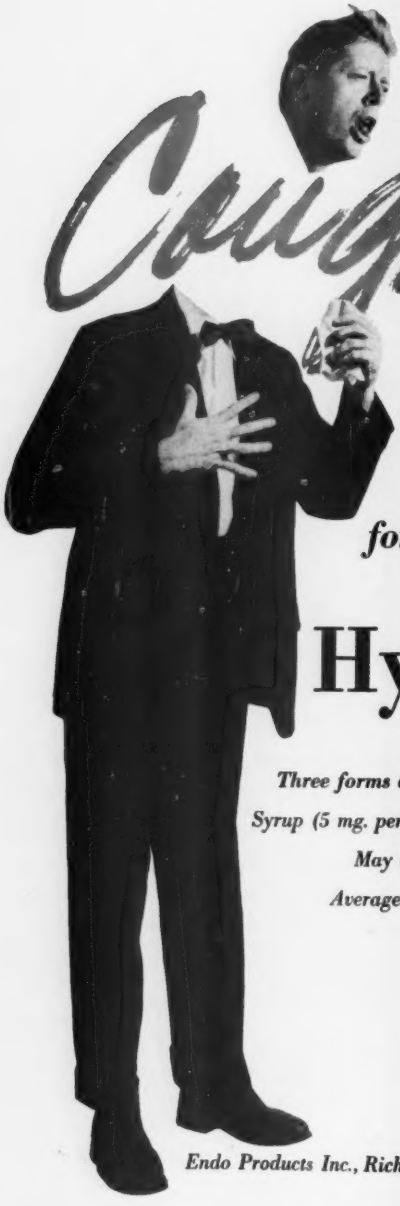

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Figure 1

on an ordinary mattress.

Hospital X-ray, 128-pound, 28-year old female, lying on her back on an ordinary mattress supported by a bedboard. Note that the spine and bone structure sink well below the horizontal top edge of the innerspring, with accompanying muscle strain.

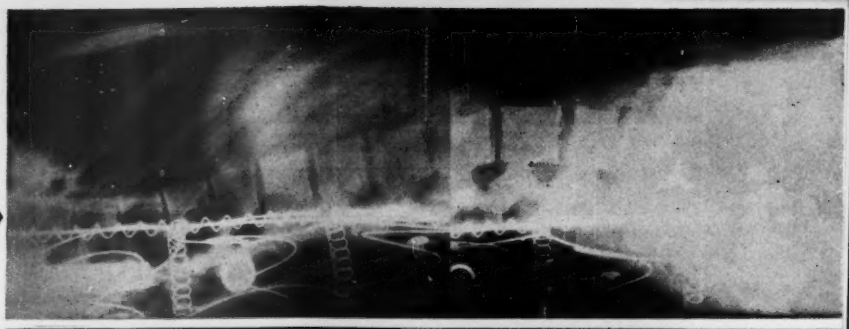

Figure 2

on Firmbak Flexiboard mattress.

Hospital X-ray, same 128-pound, 28-year old female as in Figure 1, lying on her back on the Firmbak Flexiboard mattress. Compare position of spine and bone structure with Figure 1. Support is provided by the mattress itself, permitting the muscles to rest.

Arrows indicate top of mattress.

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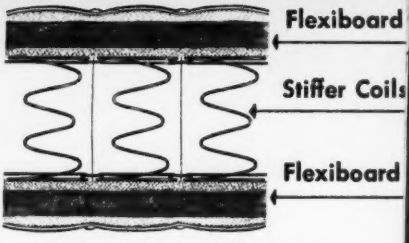

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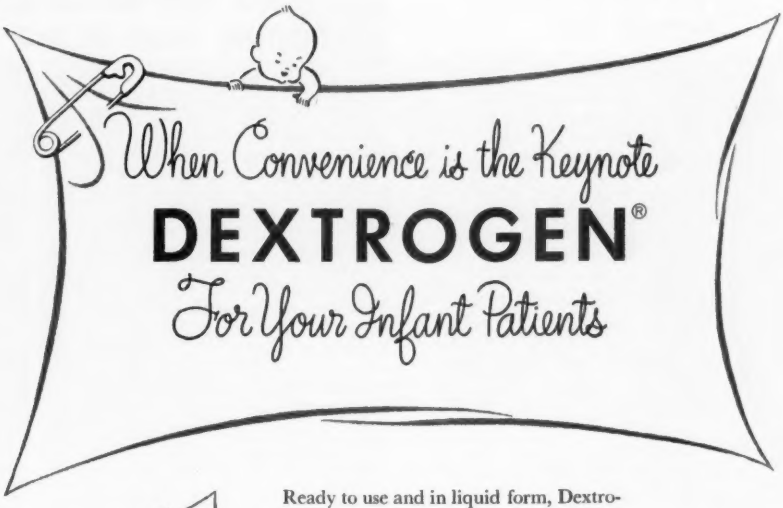

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Head Pain as a Diagnostic Lead

Frequently the presence of head pain is overlooked. The physician learns of it only if he has made an effort to elicit the information. Since the etiology of the pain is the basis of rational management, the patient should be warned against taking medication before diagnosis is made.

Friedman[1] deplores the tendency to call any chronic recurring headache migraine. Careful history-taking and full physical and neurological examinations are essential for accurate diagnosis. A good starting point is a description of the headache — its character, laterality, frequency and intensity.[2]

The following chart gives briefly the primary diagnostic leads and treatment for the most common types of headache.

Etiology of Headache	Primary Diagnostic Data	Primary Therapy
Inflammatory e.g., Meningitis Abscess	Inflammation of intracranial structures; fever; leucocytosis; bacteriologic diag.	Specific: sulfonamides and antibiotics. Symptomatic: analgesics.
Tumor	Pain varies as spinal press. changes; skull X-ray.	Specific: surgery. Symptomatic, analgesics &/or hypnotics.
Sinusitis	Sinus congestion and infection; cloudy X-ray.	Specific: antibiotics and drainage. Symptomatic: analgesics.
Hypertensive	Hypertension present but pain not related to b.p. level; Dihydroergotamine. relieves pain.	General hypertension therapy; sedation. Symptomatic: analgesics.
Migraine & other vascular headaches	Headache: recurrent, intense, throbbing. No organic causation; migraine in family; patient: energetic, perfectionist. Visual prodromata; g-i. upset during headache.	To abort attack: oral ergotamine plus caffeine. General: adjustment to minimize nervous stress.

Data here tabulated is from: Wolf, G., Jr.,[3] and Friedman, A. P.[4]

Cecil[5] ranks vascular headaches, e.g., migraine and tension headaches, as the most commonly encountered of all. Because of their functional nature and usual recurrence at frequent intervals, they present a long-term therapeutic problem.

Therapy is conducted along two lines:

1) Psychotherapy to reduce the frequency of attacks. This consists mainly of advice on emotional adjustment to stressful situations and guidance toward a good balance between work and relaxation.

2) Treatment of the distressing attack to prevent the usual period of incapacitation. Many investigators have reported that ergotamine preparations are effective for relief of the acute migraine attack in 80% of cases.[1,6] *The drug is given immediately when an attack is approaching and dosage adjusted to the needs of the individual.*

1. Friedman, A. P. and von Storch, T.: 99th A.M.A. Session, June 1950. 2. Butler, S. and Hall, F.: M. Clin. N. Amer., p. 1439 (Sept.) 1949. 3. Wolf, G., Jr.: M. J. 54:25, 1951. 4. Friedman, A. P. and Conn, H. T.: Current Therapy, 1950, p. 563; Saunders Co., Phila. 5. Cecil, R. L.: A Textbook of Medicine, ed. 7, 1948, p. 1483; Saunders Co., Phila. 6. Horton, B. et al: Staff Meet. of Mayo Clinic 20:241, 1945.

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AN APPRAISAL OF THE NEWER ELECTROCARDIOGRAPHY: CORRELATIONS IN ONE HUNDRED AND FIFTY CONSECUTIVE AUTOPSIED CASES*

HAROLD D. LEVINE, M.D.,† AND EDWARD PHILLIPS, M.D.‡

BOSTON

LARGELY as a result of the brilliant fundamental studies of Wilson and the Ann Arbor school, the last decade has witnessed a large-scale change in electrocardiograph technics and in the thoroughness with which electrocardiograms are recorded. Whereas routine studies formerly included the three conventional bipolar extremity leads of Einthoven and a single or perhaps two "precordial" leads, likewise utilizing a bipolar technic, the recent trend, except in a few clinics, has been to include the three conventional limb leads, three unipolar limb leads and six (or in some quarters seven) unipolar chest leads. It is the current consensus, as indicated by a careful reading of the literature and discussion with a large number of competent electrocardiographers, that the newer methodology represents a distinct advance over the old. Certain advantages of the Wilsonian electrocardiography have been pointed out. By exploring a more extensive area of the precordium it has been possible to detect old infarcts of small size as well as anteroseptal infarcts that because of their projection in an anteroposterior direction might escape detection in the extremity leads. It has helped to separate the alterations due to changes in the position of the heart from those due to changes resident in the heart itself. In the case of intraventricular block it has offered reliable data enabling one to ascertain whether there is delay or block in one bundle branch or the other. In the hands of some observers the use of the unipolar extremity leads has been reported as helpful in the decision of whether a Q wave in Lead III is the result of posterior myocardial infarction and has been reported as offering a clue to high lateral infarction. To our minds, however, the most important contribution of the method has been that it represents a rational rather than an empirical approach to the subject and, in the hands of most students, has led to a better *understanding* of electrocardiographic developments.

Although certain details of technic and interpretation still remain to be clarified, there is little doubt that the method represents a distinct, convincing and remarkable advance. With it, however, a widespread impression has unfortunately developed, — apparent in a reading of the literature and in discussion with students and physicians, — that the electrocardiogram has now emerged as an infallibly precise instrument of unlimited capacities. In effect, one simply presses one or two buttons, turns a crank and obtains the right answer. We have recently had occasion to review our experience with the newer technics and have found that this hope falls far short of realization.

To examine the over-all accuracy of the newer method, the records were studied of 150 consecutive patients on whom at least one complete set of tracings had been taken during their terminal illness and who were subsequently examined at autopsy. Both medical and surgical patients on the wards of the Peter Bent Brigham Hospital were included. The majority of the patients died of heart disease; this, of course, is because electrocardiograms are more likely to be taken in patients with heart disease. Other causes of death were carcinoma, blood dyscrasias, pneumonia, sepsis, trauma and exsanguination. In each case the electrocardiographic diagnosis was tabulated without knowledge of the post-mortem findings and, conversely, the post-mortem findings were tabulated without knowledge of the electrocardiographic diagnosis. In this way we believe that we obtained a representative and objective picture of the over-all accuracy of the electrocardiographic method.

The electrocardiographic criteria used in this study were those set forth by Wilson and his group.[1, 2] No attempt was made in this study to utilize vectorcardiographic methods. The autopsies were performed carefully by members of the Department of Pathology who were keenly interested in this study. Examination of the heart varied somewhat in the detail in which it was carried out,

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School.
This study was partly supported by a grant from the Anna R. Lown Cardiac Research Fund.
†Clinical associate in medicine, Harvard Medical School; associate in medicine, Peter Bent Brigham Hospital.

‡Formerly, research fellow in medicine, Harvard Medical School; instructor in medicine, University of Southern California School of Medicine and College of Medical Evangelists.

but in general the technic included the conventional gross and microscopical examination with serial transverse sections, 1 cm. apart, made from the apex to the base of the heart. Numerous additional microscopical sections were also examined. Injection-with-dissection studies were not included. In the evaluation of hypertrophy of the ventricles consideration was given to the weight of the heart and the thickness of each ventricle and of the papillary muscles. It was not practical in this study to obtain the weight of the free walls of the individual ventricles.

The diagnoses given below were made objectively by the electrocardiographer, solely on the basis of the tracings. They might or might not, in a given case, correspond to the clinical diagnosis.

Anterior Myocardial Infarcts

Electrocardiographic Diagnosis

In 19 cases the electrocardiographic diagnosis of infarction of the anterior portion of the myocardium was made. In 15 the diagnosis was made during the acute stage and in 4 after a presumed original attack. In 4 cases the patient was studied electrocardiographically several months after, as well as during, the acute episode. In all 15 cases in which acute infarction of the anterior wall was diagnosed, the autopsy substantiated the diagnosis. However, in one of these cases, which was studied on two admissions, the existence of the acute infarction diagnosed during the first admission was proved, but a more recent infarct adjacent to the original lesion was not detected electrocardiographically.

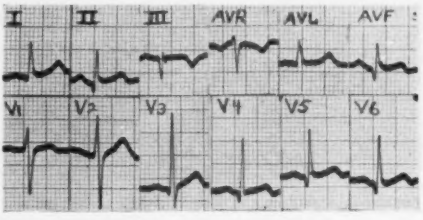

Figure 1. *Old Anteroseptal Infarct Simulating Old Posterior Infarct in a 66-Year-Old Woman Who Died of Cerebral Hemorrhage.*

Note deep Q waves in Leads II, III and aVF. Autopsy showed 2-by-2-cm. old infarct in anterior part of septum but no posterior infarct.

Of the 4 cases in which an old anterior infarct was diagnosed, post-mortem examination corroborated the diagnosis in 3. No infarct or scar was found in the other. The electrocardiographic diagnosis of anterior infarction in the latter case was based on a decrease in the height of the R wave in precordial Leads V_1 to V_3 and an absent R wave in V_2.

Anatomical Diagnosis

Anterior infarcts were found at autopsy in 32 cases. In 20 cases the patient was studied during the acute illness. Those who survived the acute illness were studied again before death. Thus the electrocardiographic changes and the lesions found at autopsy could be properly correlated. The correct electrocardiographic diagnosis of acute anterior infarction was made in 15 of the cases — in one of these in the presence of left-bundle-branch block. The electrocardiogram missed the acute infarct in 5 cases. In 3 of the latter group electrocardiograms were abnormal but showed nonspecific, nondiagnostic changes; in 1 the presence of auricular flutter and right-bundle-branch block made it impossible to distinguish decisive QRS-complex or T-wave changes. In another the typical electrocardiographic changes of left-ventricular hypertrophy were present; hypertrophy was also found at autopsy. All these infarcts were of appreciable size, being described as "large" or as exceeding 2 by 3.5 cm.

There were 12 cases with old healed anterior myocardial infarcts. The electrocardiographic diagnosis was made correctly in only 3 cases. Of the 9 cases that were missed by electrocardiography, 4 showed characteristic changes of left-ventricular hypertrophy, 1 had left-bundle-branch block, 1 showed low voltage, 1 showed an electrocardiogram suggestive of old posterior (?posterolateral) infarction (Fig. 1), and in 2 the typical changes of recent posterior infarction were present. The size of the scars in this group varied from 2 to 5 cm. in diameter and was large enough in one case to extend to the anterior wall of the right ventricle and in another to the lateral wall of the left ventricle.

It appears from these data that the diagnosis of acute anterior infarction can be made with a much greater degree of accuracy than that of old anterior infarction. In fact, the majority of old anterior scars are not diagnosed. Left-ventricular hypertrophy, which is not infrequently associated with healed myocardial infarction, produces low to absent R waves in Leads V_1 through V_3 or V_4, thereby obscuring or confusing the QRS-complex changes due to old anterior infarction. In such cases the diagnosis of old anterior infarction cannot be made with confidence.

Posterior Myocardial Infarcts

Electrocardiographic Diagnosis

The electrocardiographic diagnosis of acute posterior myocardial infarction was made in 14 cases; that of old posterior infarction, in 2 instances. In all these cases the electrocardiographic diagnosis was confirmed by post-mortem examination. The presence of depressed ST segments in Leads V_3 through V_6 in the absence of a Q wave in Lead aVF in one of these cases raised the question of sub-

endocardial infarction of the anterior wall, but the alternate possibility of posterior infarction was favored. In a second case the diagnosis of acute posterior infarction was made in the presence of right-bundle-branch block. Another case was of interest in that although no Q wave was present in Lead aVF there were ST-segment changes in Leads aVF, I, II and III that enabled the electrocardiographer to diagnose posterior infarction; a prominent Q wave was present in Lead III (Fig. 2). Had the patient lived, the Q wave in Lead aVF might well have developed as the RS–T displacement decreased.

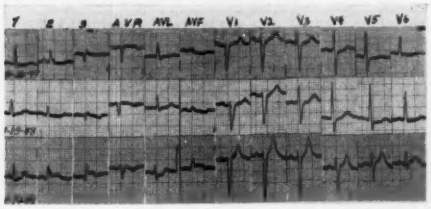

FIGURE 2. *Acute Posterior Infarction without Prominent Q Wave in Lead aVF in a 63-Year-Old Man with Angina and Hypertensive Heart Disease.*

Upper tracing shows minor ST-segment and T-wave abnormalities. Middle tracing shows minor RS-T-segment changes in Leads V_4 and V_5 during an attack of angina. Lower tracing, taken shortly after onset of epigastric pain and shock, shows typical ST-segment and T-wave changes in standard and unipolar limb leads, no significant Q wave in Lead aVF and tall T waves in Leads V_2 and V_3. Autopsy showed perforated duodenal ulcer and acute posterior myocardial infarct.

Two cases of acute posterior infarction showed no Q wave in Lead aVF. The proper electrocardiographic diagnosis was made on the basis of other changes.

Anatomical Diagnosis

In 29 cases autopsy revealed posterior myocardial infarction. Eighteen of these were recent; 11 consisted of old scars. Fourteen of the 18 acute infarcts were properly diagnosed and 4 were missed. In 3 of the 4 cases in which the diagnosis was not made the electrocardiogram showed marked left-ventricular hypertrophy. In one of these the additional electrocardiographic anatomic diagnosis of old anterior myocardial infarction was made correctly. In the fourth, acute cor pulmonale was suspected (further described under "septal infarct").

In the 11 cases of old posterior infarction the electrocardiographic diagnosis was made in only 2, but all the others showed abnormal electrocardiograms. One showed auricular flutter, one left-bundle-branch block, one incomplete right-bundle-branch block with left-ventricular hypertrophy and one acute anterior infarction (confirmed). Four other cases corresponded to left-ventricular hypertrophy; 2 of these had additional anterior infarctions that were also missed electrocardiographically. The eighth case deserves special consideration. The patient was an eighty-four-year-old man who died of progressive heart failure. He gave no history suggestive of angina or previous coronary occlusion. The electrocardiogram (Fig. 3) showed a prominent Q wave in Lead III, measuring 0.03 second in duration, but none in Lead II. T waves were low in Lead I, flat in Lead II and inverted in Lead III. Unipolar limb leads showed the heart in an intermediate position; there was no Q wave in Lead aVF. Unipolar chest leads were not remarkable. The prominent Q wave in Lead III was discounted as an effect of the R wave in Lead aVL rather than as a result of posterior myocardial infarction. At autopsy a scar measuring 1.5 cm. in diameter was found in the posterior wall of the left ventricle. Even with the knowledge of the post-mortem findings, it would be difficult to attribute the Q wave in Lead III to the old posterior scar rather than to the R wave in Lead aVL. It is

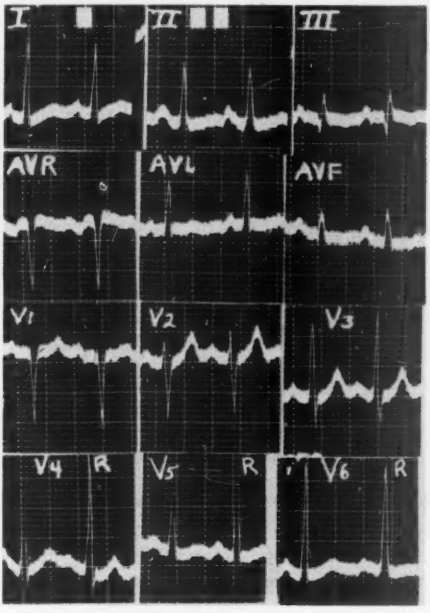

FIGURE 3. *Old Posterior Myocardial Infarct without Prominent Q Wave in Lead aVF in an 84-Year-Old Man with Progressive Heart Failure.*

Autopsy showed a scar 1.5 cm. in diameter on posterior wall of left ventricle.

thought that a diagnosis of posterior infarction on the basis of the three standard leads would have been fortuitous.

It is important to note that of the 12 posterior infarcts that were missed only one was less than 2 cm. in diameter.

As in the case of anterior infarctions, the diagnosis of acute posterior myocardial infarction is apparently much more accurate than that of old scarring. The electrocardiographic diagnosis of acute infarction was confirmed by autopsy in every case. Seventy-seven per cent of all (38) acute infarcts found at autopsy were detected electrocardiographically. This parallels the experience of Feil, Cushing and Hardesty,[3] who used two chest leads. The absence of a Q wave in Lead aVF does not rule out the diagnosis of posterior infarction; 4 of our cases showed no significant Q wave in Lead aVF. It seems possible that the failure to detect a Q wave in Lead aVF in posterior infarction may in some cases be related to a horizontal position of the heart. It is of interest to note that 8 of the 13 posterior infarcts that were missed by electrocardiography showed tracings typical of left-ventricular hypertrophy. In discussing the discrepancy between the theoretical and practical significance of a Q wave in Lead III and one in Lead aVF, Fiske[4] recently suggested that the R wave in Lead aVL may be more than a passive contributor to the formation of the Q wave in Lead III.

High Lateral Infarcts

In this study no instances of "pure" high lateral infarcts were encountered; there were a few cases in which high lateral infarction represented a portion of large posterolateral or anterolateral infarcts.

Septal Myocardial Infarcts

Because of current interest in the diagnosis of septal infarction[5-7] the electrocardiograms of 12 patients in whom autopsy showed *prominent* recent or old infarction of the interventricular septum were re-examined. The infarction involved the anterior part of the interventricular septum in 5 patients, the posterior part in 6 patients. The twelfth patient had a subendocardial infarct involving the anterior wall of the left ventricle and the left side of the entire interventricular septum and had an associated transmural infarction of the posterior wall of the left ventricle.

The infarct was acute in 3 of the 5 cases with involvement of the anterior part of the septum. One of these septal infarcts extended into the anterior wall of the left ventricle. This patient had right-bundle-branch block varying from incomplete to complete. He also had chronic cor pulmonale. The second had grossly obvious acute infarcts of the midportion of the septum and of the lateral wall of the left ventricle. The electrocardiogram showed a very low R wave in Leads V_1 through V_4, in retrospect consistent with but not diagnostic of anterior myocardial infarction. There was anatomic but no electrocardiographic evidence of left-ventricular hypertrophy in this case. The diagnosis of acute anteroseptal infarction was made in the third case in spite of the presence of left-bundle-branch block because of sequential changes in Leads V_1 through V_4.

There were 2 old infarcts of the anterior part of the interventricular septum, both extending into the free wall. One of these patients had a normal electrocardiogram; the other had left-bundle-branch block. The latter patient also had an aneurysm of the anterior wall.

Five of the 6 infarcts involving the posterior portion of the septum were acute. Two of these showed left-bundle-branch block; one showed additional first-degree heart block and at autopsy was found to have a ruptured septum. The fourth case showed intermittent complete heart block. The fifth showed no conduction defect. Four of these five acute infarcts showed typical electrocardiographic evidence of posterior infarction; in one the changes were superimposed on right-bundle-branch block. The fifth case showed a deep S wave and a depressed ST segment in Lead I and an elevated ST segment and a biphasic T wave in Lead III, but on the basis of a small Q wave in Lead aVF the diagnosis of acute cor pulmonale[8] was incorrectly considered more likely than acute posterior infarction. The single case of old infarction of the posterior part of the septum showed left-bundle-branch block. At autopsy there was a scar measuring 3 by 4 cm. in the posterior half of the septum.

It seems from these observations that acute infarction of the posterior aspect of the septum is likely to give rise to suggestive or diagnostic electrocardiographic changes of posterior myocardial infarction. Definitive electrocardiographic changes were much less commonly encountered with infarction of the anterior part of the septum. With involvement of either the anterior or the posterior part of the septum bundle-branch block was quite common. In the entire group of 12 patients with septal infarcts 4 showed left-bundle-branch block and 3 showed right-bundle-branch block. The various degrees of auriculoventricular block were encountered exclusively in the group with infarction of the posterior part of the septum. These observations are in close agreement with those recently reported by Osher and Wolff,[7] who utilized the injection-dissection technic of Schlesinger in a larger group of cases of septal infarction. During the present study no case was observed of infarction of the entire septum of the type described by Roesler and Dressler.[9]

Subendocardial Myocardial Infarcts

Although it is known that most infarcts are predominantly subendocardial, in occasional cases the

subendocardium is exclusively involved. Five such cases were found in the present study. Since these cases are of considerable theoretical interest, they have been more fully considered in a separate communication.[10] The electrocardiogram in these cases showed, in one or more of the precordial leads and occasionally in Leads aVL or aVF as well, persistent depression of the ST segment, followed by upright T waves, associated with an elevated ST segment in Lead aVR and no abnormal Q wave in Lead aVF.

Coronary-Artery Disease without Myocardial Infarcts

In addition to the patients with myocardial infarcts there were 14 who showed moderate to marked coronary-artery disease at autopsy. This consisted of tortuosity, calcific deposition and narrowing of the lumen of a major branch. The myocardium was normal on gross and microscopical examination in 5 of these patients. Grossly visible fine, scattered scarring was present in 4. The other 5 showed some fibrosis only on careful microscopical examination.

The electrocardiogram was normal in 3 of these 14 patients; 2 of them showed microscopic fibrosis and the third had a normal myocardium at autopsy. Three patients had electrocardiograms characteristic of left-ventricular hypertrophy, 2 showed evidence of left-bundle-branch block and 6 showed abnormal nonspecific electrocardiograms. This experience is typical of that described in the literature and does not require further comment.

Left-Ventricular Hypertrophy

Electrocardiographic Diagnosis

The diagnosis of left-ventricular hypertrophy was made in 38 patients by the criteria of Wilson and his co-workers.[1, 2] In these cases the R wave in Leads V_1 through V_3 was very small or absent, the S wave in Leads V_1 through V_3 was large and the transitional zone was usually displaced to the left. The R wave to the left of the transitional zone (usually Leads V_4 through V_6) was often preceded by a Q wave and showed high voltage with a late intrinsicoid deflection. The T waves were inverted in the leads from the left precordium and the ST segments were usually depressed.

The additional diagnosis of myocardial infarction was made in 3 of these patients, and in 2 others concomitant right-ventricular hypertrophy was correctly diagnosed. Fourteen other patients in this group also had additional right-ventricular hypertrophy at autopsy, but only the left-ventricular hypertrophy was diagnosed by electrocardiography. The bulk of these patients had hypertensive heart disease with congestive failure. It is pertinent to note again that in 13 of the 38 patients in whom the diagnosis of left-ventricular hypertrophy was correctly made 15 myocardial infarcts were found at autopsy; only 3 of these were correctly diagnosed by electrocardiography. These cases have been further analyzed under "myocardial infarction."

Our experience shows that left-ventricular hypertrophy was invariably found at autopsy when it was diagnosed electrocardiographically, but the presence of additional right-ventricular hypertrophy or old myocardial infarction was usually missed by the electrocardiogram.

Anatomic Diagnosis

There were 37 cases in which pure left-ventricular hypertrophy was found at autopsy. The electrocardiogram correctly anticipated this finding in 25 but did not do so in the other 12 cases.

These 12 are considerable interest and were analyzed in detail. Two showed left-bundle-branch block, one showed right-bundle-branch block and two had normal electrocardiograms. The electrocardiogram was abnormal in the other 7, but decisive criteria for the diagnosis of left-ventricular hypertrophy were lacking. In general the high voltage to be expected in the precordial leads overlying the left ventricle was not present. In 5 of the latter 7 cases the heart was in the vertical electrical position (in 2 the apex was apparently displaced posteriorly), hence the transitional zone was not actually crossed, and true left-ventricular potentials were not obtained in Lead V_6. The electrocardiogram in 3 of these was considered very suggestive of left-ventricular hypertrophy. In retrospect, it seems that the diagnosis might have been made in some of these patients if additional tracings had been taken one or two intercostal spaces higher or had been recorded farther to the left in the posterior axillary or midscapular line.

Combined Ventricular Hypertrophy

In the entire group of 150 cases, 26 showed combined left- and right-ventricular hypertrophy at autopsy. As stated above, only 2 of these were correctly diagnosed by electrocardiography. The electrocardiogram showed left-ventricular hypertrophy in 12 cases. Miscellaneous electrocardiographic diagnoses were made in the other 12 cases: Two had right-bundle-branch block, 2 showed old anterior myocardial infarction confirmed at autopsy, 7 had nonspecific abnormal electrocardiograms and one showed right-ventricular hypertrophy. True left-ventricular potentials were not obtained in the latter case; here again, if precordial leads had been taken farther to the left combined hypertrophy might have been anticipated.

It seems that combined hypertrophy is rarely detected in the electrocardiogram. In about 50 per cent of these cases the electrocardiogram showed left-ventricular hypertrophy, and bundle-branch block and nonspecific abnormalities were seen in the others. It is believed that the accuracy of diagnosis will be increased if true right- and left-ventricular potentials are obtained by taking a sufficient

number of additional unipolar chest leads in selected cases.

Right-Ventricular Hypertrophy

The electrocardiographic diagnosis of right-ventricular hypertrophy[1, 2, 11] was made in 8 patients and was confirmed at autopsy in all. The R wave was prominent in Lead V_1 or in Leads V_1 and V_2 and generally decreased in height from Lead V_1 to Lead V_6. The R wave actually disappeared in Lead V_6 in two cases, giving an appearance reminiscent of old localized anteroseptal myocardial infarction (Fig. 4). A Q wave was present in Lead V_1 or in Leads V_1 and V_2 in all but one case. The intrinsicoid deflection was late over the right ventricle, varying from 0.03 to 0.07 second. The T wave in Lead V_1 or in Leads V_1 and V_2 was inverted, and the ST segment was usually depressed in these leads. Lead aVR showed a prominent R′ wave or prominent R wave preceded by a Q wave in seven cases (Fig. 5). The exception was the only one in which right-ventricular hypertrophy might have been suspected from the conventional limb leads, which showed right-axis deviation with depression of the ST segment and inversion of the T wave in Leads II and III. This case showed the earliest intrinsicoid ventricular deflection in Lead V_1 (0.03 second).

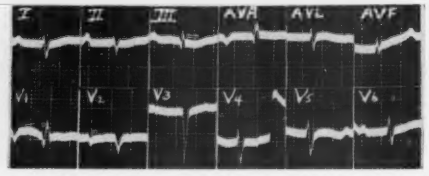

Figure 4. *Right-Ventricular Hypertrophy with Tracing Resembling Old Anterior Infarct in a 33-Year-Old Man with Chronic Cor Pulmonale due to Lifelong Asthma.*

Autopsy showed pulmonary emphysema, peripheral congestion and a thick right ventricle (0.7 cm.) but no myocardial infarct.

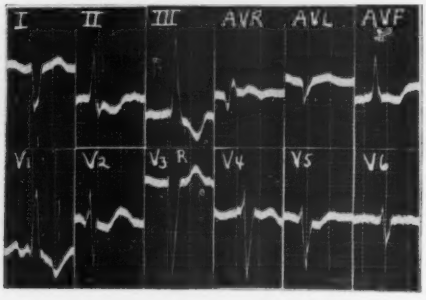

Figure 5. *Right-Ventricular Hypertrophy in a 39-Year-Old Man with Mitral Stenosis.*

Autopsy showed that the mitral valve admitted only the end of the probe.

In the evaluation of a prominent R wave in Lead V_1 or V_2, particular care was taken to be certain that this was not due to counterclockwise rotation of the heart on its longitudinal axis. In such cases the S wave is usually prominent, the intrinsicoid deflection of the R wave is not delayed and the T waves are not inverted in V_1 or V_2.[11, 12]

In 2 additional cases post-mortem examination showed right-ventricular hypertrophy, but the diagnosis was not made electrocardiographically. One was a case of Lutembacher's syndrome that showed typical right-bundle-branch block. The right ventricle measured 0.9 cm. in thickness. The electrocardiogram showed a very high R′ wave in Lead V_1 instead of an M-shaped QRS complex with so-called "septal" and "free wall" components of equal heights (Fig. 6). This is said to be suggestive of combined right-ventricular hypertrophy and right-bundle-branch block.[2] The second case showed nonspecific electrocardiographic changes with inversion of the T wave in Leads V_1 and V_2, absent R waves in Leads V_1 and V_2 and a small R wave in Lead V_6. This tracing was more suggestive of left-ventricular than of right-ventricular hypertrophy.

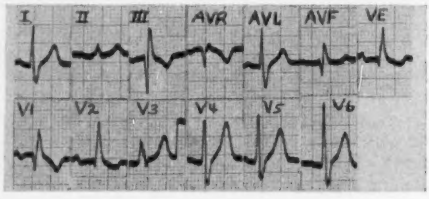

Figure 6. *Right-Bundle-Branch Block with Right-Ventricular Hypertrophy in a 57-Year-Old Man with Lutembacher's Syndrome.*

Autopsy revealed that the right ventricle was 0.9 cm. thick.

From these data it is apparent that when definitive electrocardiographic criteria for right-ventricular hypertrophy are present this diagnosis will be substantiated at autopsy.

Acute Cor Pulmonale

The diagnosis of acute cor pulmonale was made in 8 cases on electrocardiographic grounds. Post-mortem examination confirmed this diagnosis in 7. The eighth had acute posterior myocardial infarction. In a ninth case, acute cor pulmonale was favored over subendocardial infarction, but the latter was found at autopsy. Another patient had

pulmonary embolism at autopsy, but electrocardiographic examination, made during what might be considered an opportune time, failed to make the diagnosis.

Four cases showed characteristic changes in the standard limb leads.[18] One showed changes limited to the unipolar chest leads, and in 2 others equivocal changes in the standard leads were supported by characteristic changes in the chest leads. Four of these showed incomplete right-bundle-branch block. An interesting finding was the presence of an abnormal Q wave in Lead aVF in 2 patients in this group with acute cor pulmonale.

Bundle-Branch Block

There were 15 cases in which the diagnosis of bundle-branch block was made. Nine of these were right-bundle-branch block and 6 were left-bundle-branch block. In the group with right-bundle-branch block 3 were complete, 4 were incomplete and 2 varied from incomplete to complete right-bundle-branch block. The anatomic findings were quite variable; 3 showed myocardial infarction, 2 had pulmonary embolism, 3 had combined ventricular hypertrophy, 3 had left-ventricular hypertrophy and 1 had right-ventricular hypertrophy. (Some of these conditions were coexistent, as, for instance, pulmonary embolism and ventricular hypertrophy.)

In two cases (Fig. 6 and 7) the secondary R wave (R′) over the right ventricle was very tall. Wilson[2] stated that this might suggest right-ventricular hypertrophy complicated by right-bundle-branch block. Each of these cases showed a thick right ventricle at autopsy, the measurements being 0.9 and 0.8 cm. However, all cases with right-bundle-branch block and right-ventricular hypertrophy do not show this prominent R′; two cases with combined ventricular hypertrophy showed low M-shaped QRS complexes over the right ventricle. In the remaining 5 cases there was no tall R′ and no right-ventricular hypertrophy.

Of the 6 patients with left-bundle-branch block, 2 showed posterior myocardial infarction at autopsy, 2 had anterior myocardial infarction and the other 2 had coronary-artery disease without infarct and left-ventricular hypertrophy, respectively.

Aside from the association of bundle-branch block with septal infarction, this study proves nothing with regard to bundle-branch block, which is a purely electrocardiographic diagnosis.

Auriculoventricular Heart Block

In addition to the cases of auriculoventricular block described under myocardial infarction, there were 5 cases of auriculoventricular block and one with interference and dissociation. Two of these had first-degree block and right-ventricular hypertrophy. A third case of first-degree block was seen in a sixty-seven-year-old woman with pneumonia whose electrocardiograms were otherwise normal. Her heart was normal at autopsy. The fourth patient was a forty-six-year-old woman with complete heart block and Adams–Stokes attacks due to paroxysmal ventricular tachycardia who showed frequent ventricular premature beats between attacks. The electrocardiograms showed no evidence of myocardial infarction. The terminal mechanism was ventricular fibrillation. At autopsy her heart appeared to be normal. The right coronary artery supplied all the coronary arterial tree except for the anterior part of the left ventricle, which was supplied by the left coronary artery. The latter showed minimal intimal thickening microscopically. The fifth patient had auricular fibrillation, idioventricular rhythm and occasional ventricular premature beats. Post-mortem examination showed a rheumatic myocarditis, rheumatic coronary arteritis with thrombosis and old mitral valvulitis. The sixth patient had interference and dissociation on the day of death, when the blood urea nitrogen level rose to 65 mg. per 100 cc. Autopsy showed left-ventricular hypertrophy and old posterior myocardial infarction.

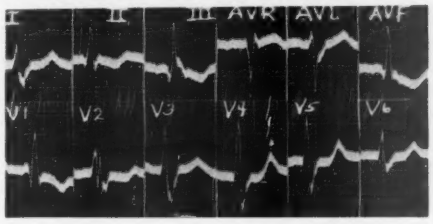

Figure 7. *Right-Bundle-Branch Block with Right-Ventricular Hypertrophy in a 73-Year-Old Man with Angina. Autopsy showed combined ventricular hypertrophy, the heart weighing 500 gm. The left ventricle was 2.0 cm. and the right was 0.8 cm. thick.*

Nonspecific Abnormal Electrocardiograms

Thirty-eight patients had electrocardiograms that were abnormal but nonspecific. The principal changes noted were flat or inverted T waves in Lead I or Lead II or both frequently associated with similar changes in the leads from the left precordium. A flat or inverted T wave in Lead aVL or aVF was not of itself considered abnormal. Also included in this group were simple sinus tachycardia with heart rate exceeding 120 beats per minute (2 cases), intraventricular block (2 cases) and low-voltage electrocardiograms (3 cases).

The anatomic findings in this group were: left-ventricular hypertrophy, 8 cases; myocardial infarction, 7 cases; combined ventricular hypertrophy, 6 cases; coronary arteriosclerosis without infarction,

6 cases; uremic pericarditis, 4 cases; hepatic cirrhosis, 2 cases (one associated with pneumonia, the other with probable beri-beri); hemochromatosis of the heart, 2 cases; metastatic tumor of the heart or pericardium, 3 cases (2 were reticulum-cell sarcoma and one was carcinoma of the lung); and 1 case each of rheumatic myocarditis, phosphorus poisoning and right-ventricular hypertrophy. In 4 cases the heart appeared to be perfectly normal at autopsy. One of these patients had acute disseminated lupus erythematosus with anemia and uremia, and another had acute hemorrhagic pancreatitis; both showed low-voltage electrocardiograms only. The remaining 2 had anemia associated with carcinomatosis, the hemoglobin levels being 7 and 8 gm. per 100 cc.; the electrocardiograms showed T-wave changes.

Pericarditis

Uremic pericarditis was found at autopsy in 7 patients. Four of these had abnormal nonspecific electrocardiograms, and 3 showed left-ventricular hypertrophy. In only 1 were we able to detect changes suspicious of pericarditis — and then only in retrospect. These findings are similar to those recorded in the literature.

Myocarditis

There were 2 cases in which the diagnosis of acute myocarditis was made at autopsy. One is the patient with rheumatic arteritis, described above, whose electrocardiogram showed nonspecific changes. The other was a twenty-six-year-old man who died during an attack of acute rheumatic fever. Autopsy showed a large heart with granulomatous lesions in the myocardium consistent with rheumatic myocarditis. The electrocardiograms showed combined ventricular hypertrophy in this case.

The Electrocardiograms in Other Anatomic Lesions

Eight patients showed miscellaneous findings at autopsy. Two showed hepatic cirrhosis, and three had metastatic tumor of the heart and pericardium. These have been discussed under abnormal nonspecific electrocardiograms. Three patients had hemochromatosis; in 2 of these the heart showed pigmentary and fibrotic changes said to be characteristic of hemochromatosis of the heart.[14] The latter 2 patients had abnormal nonspecific electrocardiograms. One patient died of phosphorus poisoning. Autopsy showed organic changes characteristic of this condition and a subendocardial hemorrhage on the left side of the interventricular septum. The electrocardiogram showed nonspecific T-wave changes similar to those described in the literature.[15, 16]

Normal Electrocardiograms

Normal electrocardiograms were obtained in 15 patients. Nine of these had normal hearts at autopsy, 3 showed coronary arteriosclerosis without infarction, 1 showed slight left-ventricular hypertrophy and another showed marked left-ventricular hypertrophy. The remaining patient died of multiple myeloma; his heart was normal in all respects except that it was heavy, weighing 510 gm., and showed edema of the heart muscle microscopically. Thus in this series a normal electrocardiogram was seldom associated with an abnormal myocardium.

Normal Hearts

Among 17 cases in which the heart was normal at autopsy 9 showed normal electrocardiograms. Five had abnormal nonspecific electrocardiograms; 3 of these had profound anemia and 1 had cirrhosis of the liver, each of which is known to produce electrocardiographic changes in the absence of anatomic lesion. The other had acute pancreatitis. Two additional patients had auriculoventricular block. One had first-degree block associated with pneumonia. The other was a case of complete heart block in which serial sections of the auriculoventricular node and bundle were not made. The final case was erroneously diagnosed as old anterior myocardial infarction. The latter 8 cases have been more fully discussed above.

These data show that in the presence of a normal heart the electrocardiogram either was normal or showed changes attributable to anemia or to toxic or chemical insults.

Discussion

This study demonstrated the high degree of accuracy of the electrocardiographic diagnosis of uncomplicated acute myocardial infarction, of uncomplicated left-ventricular or right-ventricular hypertrophy and of acute cor pulmonale. The electrocardiographic diagnosis of combined ventricular hypertrophy was inaccurate, probably because in this series of cases the right-ventricular hypertrophy was secondary to, and apparently electrically dominated by, left-ventricular hypertrophy. The electrocardiographic diagnosis of old myocardial infarction was quite inaccurate. It has been suggested that this may be due to the small size of the scar or to the fact that the scar may not be strategically located to produce electrical effects. The electrocardiographic diagnosis of multiple infarcts of varying age was also inaccurate. This may be due to the fact that infarcts located on opposite walls might extinguish one another electrically or to predominance of the electrical effect of one infarct over that of another with the result that the changes induced by the latter become submerged in the former.

Abnormal but nonspecific electrocardiograms, showing, for example, T-wave inversion or low voltage, were recorded with many pathologic conditions of the heart, but normal electrocardiograms generally signified normal hearts. Normal hearts, on the other hand, inscribed normal or abnormal electrocardio-

grams, the latter being attributable to certain chemical or "ischemic" changes unassociated with a demonstrable anatomic lesion.

The superiority of the injection-dissection technic over the conventional incisions in the detection of myocardial infarction has been well established. Possibly excepting its failure to demonstrate subendocardial infarcts, the former is probably superior also to the method of parallel slices here employed. In our experience one cannot be certain from gross sectioning of the heart that infarction is absent. However, the principal disparity here noted consisted in the anatomic demonstration of infarcts in the absence of corresponding electrocardiographic changes. In those cases in which distinctive electrocardiographic changes were recorded, the anatomic findings were largely corroborative; the electrocardiographic findings impelled us to make numerous microscopical sections from all parts of the heart, even from regions where the gross examination did not lead us to suspect infarction. On the other hand we believe that the divergence between the injection-dissection technic and the method here employed would be in the direction of the former's picking up more infarcts in hearts that *failed* to inscribe diagnostic electrocardiographic changes. It is our impression, therefore, that the use of the more meticulous procedure might well widen rather than narrow the discrepancy between the electrocardiographic and the pathologic findings.

A direct comparison of unipolar with bipolar chest electrocardiograms was not made in this investigation. An extensive series of cases so studied, with post-mortem correlation, would be of great interest. From the present study and a review of the literature, however, it seems obvious that certain conditions can be missed by either method. This brings us back to our point of departure. It is quite clear from the present experience that the impression that the newer electrocardiography possesses unlimited accuracy is unfounded. There is still need for the employment of restraint, caution and humility in electrocardiography. The electrocardiogram, like other laboratory procedures, should be evaluated in the light of the clinical findings. In the evaluation of the individual tracing there is still the opportunity and need for the exercise of sound clinical judgment.

Summary

An electrocardiographic-pathological correlation was made in 150 consecutive patients. At least one complete set of conventional leads and unipolar extremity and chest leads was made in each case.

The electrocardiographic diagnosis of acute myocardial infarction was invariably correct. However, of all acute infarcts found at autopsy only 75 per cent were detected electrocardiographically. Only 20 per cent of old infarcts found at autopsy were correctly diagnosed electrocardiographically. Fifty per cent of those that were missed showed left-ventricular hypertrophy. No case of acute or old myocardial infarction showed a normal set of electrocardiograms. Of 12 cases of myocardial infarction involving the interventricular septum, 7 showed bundle-branch block.

The electrocardiographic diagnosis of left-ventricular hypertrophy was invariably substantiated at autopsy. However, other coexisting lesions such as right-ventricular hypertrophy or myocardial infarction were usually masked by the changes of left-ventricular hypertrophy. Twelve additional patients with left-ventricular hypertrophy did not show the typical electrocardiographic picture. Seven of these had vertical hearts and may not have been adequately explored electrically.

Only 2 out of 26 patients with combined ventricular hypertrophy were diagnosed electrocardiographically. In most cases in this group the electrocardiographic diagnosis of left-ventricular hypertrophy was made.

The electrocardiographic diagnosis of right-ventricular hypertrophy was substantiated in all 8 cases. Both patients with electrocardiograms characteristic of right-bundle-branch block and with a large secondary R wave (R′) over the right ventricle had right-ventricular hypertrophy at autopsy.

The diagnosis of acute cor pulmonale was confirmed in 7 of 8 patients in whom it was made electrocardiographically. It was missed electrocardiographically in 1 other case.

Thirty-eight patients showed nonspecific abnormal electrocardiograms. The chief anatomic diagnoses in this group were ventricular hypertrophy and coronary-artery disease with or without infarction. Ischemic, toxic or chemical changes could explain the abnormal electrocardiograms in 7 cases.

Of 15 patients presenting normal electrocardiograms, 9 had apparently normal hearts, 3 had coronary-artery disease without myocardial infarction, 2 had left-ventricular hypertrophy and 1 had unexplained edema of the heart muscle.

Of 17 normal hearts at autopsy, 9 showed normal electrocardiograms, 5 showed nonspecific changes, 2 showed auriculoventricular block and 1 was erroneously diagnosed as old anterior myocardial infarction on the basis of a decreasing R wave in Leads V_1 and V_2 and an absent R wave in Lead V_4.

The newer technics have definite theoretical advantages over the old. The superiority has been principally in the *understanding* of the electrocardiogram and in the detection of positional changes. However, since the electrocardiogram represents the composite effect of a number of factors operating simultaneously, the effect of certain changes may be obscured in the resulting tracing and thus may escape detection. Accordingly, restraint, caution, humility and sound judgment are still vital in its evaluation.

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INHALATION OF ETHYL ALCOHOL FOR PULMONARY EDEMA*

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TREATMENT of experimental pulmonary edema with ethyl alcohol as an antifoaming agent has been described by Luisada.[1] However, no clinical experience with this agent has as yet appeared in the literature. The purpose of this paper is to report the addition of ethyl-alcohol inhalation to the therapeutic regimen for pulmonary edema in man and to describe the solution of certain technical problems in the administration of this drug.

The conventional management of paroxysmal pulmonary edema has aimed at three goals: depression with morphine or other sedative drugs of the nerve centers involved in the reflex effects on lung capillaries; reduction of blood volume in the pulmonary circulation by upright posture, tourniquets, phlebotomy and positive-pressure respiration; and treatment of the basic cause of the pulmonary edema, as for example, digitalis for the failing heart, measures directed to the reduction of elevated intracranial pressure, removal of inhalants irritant to the bronchial mucosa and so forth.

Depending on the basic disturbance leading to the pulmonary edema, some of these measures are beneficial, others are contraindicated. Positive pressure may not be tolerated when there is already a positive intrapleural pressure. Morphine is dangerous when the pulmonary edema develops as a result of high intracranial pressure. In patients with myocardial infarction it is sometimes very difficult to walk the tightrope between pulmonary edema on the one hand and shock on the other. Reduction of venous return is beneficial in the former and may prove fatal in the latter.

The common denominator in all cases of pulmonary edema is the transudation of blood elements through altered alveolar capillary walls into the air spaces of the lung and the whipping of this fluid into froth by respiratory activity. Not only do these bubbles of froth interfere materially with diffusion of inspired oxygen but the volume of transudate is greatly increased by its conversion into foam. More and more of the bronchoalveolar system is occluded, gaseous exchange is impeded and the patient dies of asphyxia.

Ethyl-alcohol inhalation has been shown to be effective against epinephrine-induced pulmonary edema in the rabbit. This effectiveness is presumably due to alteration of the surface tension at the fluid-air interface, producing collapse of the foam bubbles, and to the volatility of the alcohol, which permits penetration into the finer air spaces.

The technical difficulty in administering alcohol by inhalation arose from the need to combine the alcohol with oxygen under pressure. Meter-mask equipment is not easily adaptable to inhalation of alcohol. Available humidifiers through which alcohol may be administered were found inadequate for delivery of sufficient oxygen under pressure. When oxygen is bubbled through fluid in a humidifier, so much resistance develops that although the gauge on the tank's reducing valve may indicate 13 to 15 liters per minute the actual volume of oxygen delivered may be less than 4 liters per minute. To obviate this difficulty, we tried at first to use two oxygen tanks. The oxygen from one tank ran

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through a humidifier containing the alcohol and thence to a Y tube attached to the meter mask; oxygen from the other tank flowed without any intervening resistance to the other arm of the Y tube. In this way the oxygen-alcohol mixture was delivered at more suitable pressure. Although results were satisfactory, this setup was cumbersome.

Our present equipment comprises a single tank from which oxygen is passed through a simple vaporizer. This latter is an 8-ounce bottle, half filled with 50 per cent ethyl alcohol, with a rubber stopper that holds two large-bore metal tubes. One of these tubes reaches to the bottom of the bottle and delivers oxygen, which bubbles through the alcohol; the other tube is above the fluid level and carries the alcohol-laden oxygen to the meter mask. All sprayers and filters are removed so that loss of pressure is minimized. This equipment can be easily and inexpensively improvised wherever oxygen therapy is practiced.

Case Reports

Case 1. E. H., a 58-year-old man, was in severe and intractable congestive failure attributed to constrictive pericarditis. Under endotracheal cyclopropane anesthesia the patient was moribund; nevertheless, operation for relief of pericardial constriction was considered his only chance for survival, and thoracotomy was carried out. The patient was awake at the conclusion of the operation. He continued in shock and soon afterwards began to develop increasing pulmonary edema. During the next 2 hours he was kept alive by conventional treatment and also received norepinephrine intravenously. However, his condition steadily deteriorated, with progressive cyanosis and increasing dyspnea. Addition of alcohol inhalation to the previous regimen brought prompt and remarkable improvement. Within 20 minutes, part of which time was spent in adjusting the oxygen flow and the fit of the mask, the patient emerged from coma, becoming lucid and oriented. Dyspnea was greatly relieved, and he said that he was comfortable. The heart rate slowed and the systolic blood pressure rose from imperceptible levels to 140 mm. of mercury. For several hours the patient was maintained in this improved state. Subsequently his condition again deteriorated, and he died 7 hours later.

Post-mortem examination revealed generalized congestion of all the viscera. The lungs were remarkable in that although there was a large basal accumulation of fluid there was no foam in the tracheobronchial tree or on any cut surface of the lung.

Case 2. S. A., a 58-year-old man, had survived an extensive myocardial infarction 1 year previously. On May 25, 1951, he was brought to the emergency ward of another hospital in acute pulmonary edema. Treatment included rapid digitalization, aminophyllin, morphine, phlebotomy and administration of 100 per cent oxygen under pressure. The patient, who was in coma, did not respond to treatment and lapsed into shock. Alcohol inhalation was instituted, using the ether vaporizer on an obsolescent anesthesia machine. Within an hour the pulmonary edema cleared, and the patient regained consciousness. Thereafter he was maintained in an oxygen tent without pressure respiration or alcohol inhalation. Subsequent study disclosed that the abrupt onset of pulmonary edema had been a manifestation of a fresh myocardial infarction. Convalescence was uneventful, and the patient was eventually discharged home.

Discussion

Paroxysmal pulmonary edema may develop in the course of a wide variety of clinical situations. Many of these are reversible, and the patient may recover if he can be tided over the acute threat of asphyxia. The final outcome depends, of course, on the nature of the underlying disturbance. The two cases presented offer evidence that the addition of ethyl-alcohol inhalation favorably modified pulmonary edema that had previously resisted all other treatment and that the mechanism of improvement in man is the same as in the experimental animal — namely, the elimination of the froth in the bronchoalveolar spaces with resulting improvement in conditions for gaseous exchange. We have observed similar favorable effects of alcohol inhalation in other patients with pulmonary edema but are reporting only these cases at present, as in the others the effects of this measure alone could not be clearly separated from the effects of other therapy.

It has been demonstrated that in normal males inhalation of alcohol does not raise the alcohol concentration in the blood to a significant level. The rate of metabolic conversion apparently keeps pace with the rate of absorption.[2] On the other hand, at feasible rates of intravenous administration alcohol does not reach the lung alveoli in sufficient concentration for effective antifoaming action.[1] In our patients no adverse systemic effects of alcohol have been noted. Indeed, use of alcohol by inhalation has been consistently associated with emergence of the patient from coma or semistuporous state.

Summary

Ethyl-alcohol inhalation can be combined with pressure oxygen therapy by the use of ordinary equipment. This treatment has been effective against pulmonary edema that had resisted all other therapy. The method described should make possible more general use and evaluation of a promising new agent in the treatment of pulmonary edema.

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GASTRIC ULCER IN THE PRESCHOOL CHILD*

Report of a Case

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GASTRIC ulcer is unusual in children. This symptom complex, although first reported by Rufz[1] as early as 1843, was not successfully recognized and treated until 1909.[2, 3]

The purpose of this article is to review the literature and report a case of gastric ulcer in the preschool child. According to Proctor's[4] criteria, 41 cases of chronic gastric ulcer in children four months to fourteen years of age have been recorded in the literature.[4-9] Five occurred in preschool children (one to six years of age, inclusive) (Fig. 1*C*).

Although the etiology of gastric ulcer in children is unknown, in the 41 cases reviewed infection and malnutrition were predominant. In adults the psychogenic factors in the etiology have gained importance that may apply as well to the young. Findings by Hoff,[10] Cushing[11] and Alvarez,[12] and reports from World War II[13-16] give credence to this view. The predisposition of children to gastric ulcer is reflected in the studies of Doll and Bush,[17] Ivy,[18] Draper[19] and Winkelstein,[20] who strongly emphasize the hereditary factors in the etiology. It is believed that gastric ulcer is more prevalent in the hypersensitive, aspiring and intellectual groups subjected to emotional stress and strain and is found seldom in people leading a listless and unproductive life, as was the writer's experience with native Liberians. No ulcer symptoms were discerned in the families of 1000 native Liberians employed at an army installation during World War II.

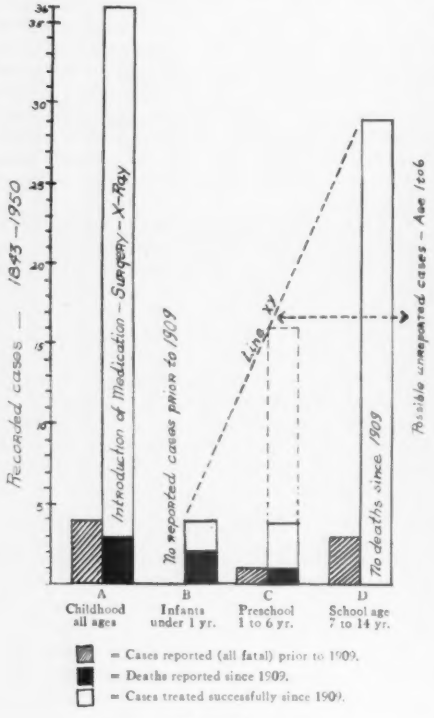
Recorded cases — 1843–1950
Introduction of Medication – Surgery – X-Ray
No reported cases prior to 1909
Line xy
No deaths since 1909
Possible unreported cases – Age 1006
A
Childhood all ages
B
Infants under 1 yr.
C
Preschool 1 to 6 yr.
D
School age 7 to 14 yr.
= Cases reported (all fatal) prior to 1909.
= Deaths reported since 1909.
= Cases treated successfully since 1909.

FIGURE 1.

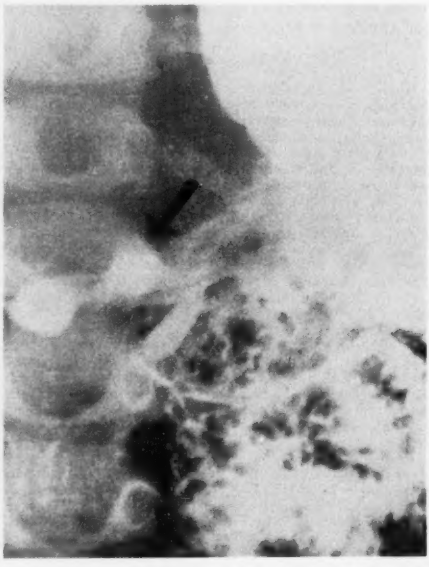

FIGURE 2. *Posteroanterior View of the Stomach. Arrow points to ulcer crater 1.2 cm. in diameter along the lesser-curvature side of the antrum.*

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Symptomatology

The pathology of this disease in children does not differ widely from that in adults, but hemorrhage[21] and perforation[5] are more common in the young. Occult blood is frequently found in the stools. Blood-tinged vomitus is often noted. The symptoms in children are usually obscure, and the history of ulcer pain characteristic of adults is seldom encountered in the young.

Case Report

J. J. K., a 5-year-old boy, was admitted to Memorial Hospital on July 29, 1950, with the complaint of fever, abdominal pain, vomiting and the passage of dark stools of 4 days' duration.

The patient had suffered recurrent abdominal pain since the age of 3 and had always had a poor appetite. He was slightly undersized and gave a history of an abnormal fear of lightning and fire. On July 4, 1950, while attending a fire-work display, he became panicky. After this incident the child was constantly ill. Four days prior to his admission to the hospital, I was called in to see the patient. Because of tenderness throughout the abdomen, vomiting, positive occult blood in the stool and a high white-cell count, the patient was referred to the hospital for x-ray studies.

Figure 3. *Right Oblique Position, Arrow Showing Collection of Barium in the Ulcer Niche on the Lesser-Curvature Side of the Antrum of the Stomach.*

The boy's father, of Greek extraction, has chronic duodenal ulcer. The mother, of Lithuanian extraction, has been treated for anxiety neurosis and often complains of gastric symptoms; x-ray findings have been negative. The boy had a tonsillectomy at the age of 4. As far as could be determined, he had had no childhood infectious diseases. The child is keen, hypersensitive and impressionable. He is an only child living with 4 adults and is, therefore, mature for his age. As the result of being supervised by 4 adult persons of varying temperaments, he has a sense of inferiority and insecurity. When playing with children of his own age he continually wants to direct their games. He lives in a "mental and emotional no-man's land." Lack of full comprehension of the adult world of the 4 adults around whom his home life revolves causes him to be unduly apprehensive. He is out of step with the life of other children, for his need for self-assertion and his mature outlook lead him to assume a dictatorial manner with boys of his own age. Obviously this maladjustment may be the underlying factor in the development of his ulcer.

X-ray examination revealed a constant collection of barium along the lesser-curvature side of the antrum of the stomach, which measured approximately 1.2 cm. in its greatest diameter, and represented a definite ulcer crater (Fig. 2, 3 and 4). The diagnosis was gastric ulcer in the antrum of the stomach.

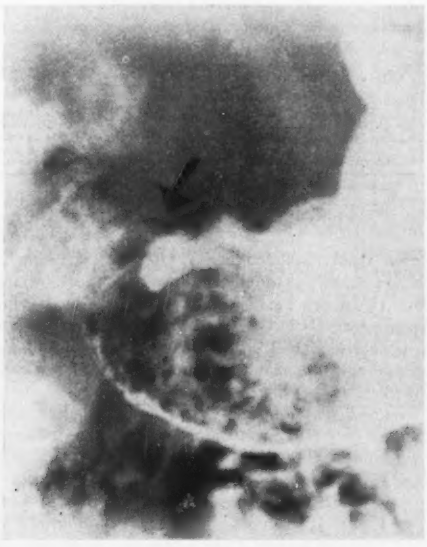

Figure 4. *Additional Film Showing Constant Collection of Barium in the Ulcer Crater on the Lesser-Curvature Side of the Antrum of the Stomach.*

The patient made an uneventful recovery after a 2-week regimen of antacid, bland diet and bed rest. A follow-up study for 8 months has revealed no return of ulcer symptoms. The patient remains on a bland diet.

Discussion

The psychogenic basis of ulcer formation has been extensively reviewed. Jordan[22] considered the primary factor to be psychosomatic. Experiments of Wolf and Wolff[23] on a human subject with a gastric fistula successfully demonstrated transient fluoroscopic changes in the stomach mucosa during studies of emotional and conflict reactions. Einhorn[24] concluded that the psychic influence of emotions, anger and shock played a causative role in ulcer formation. Dunbar[25] discussed the importance of emotional and psychic influences in the develop-

ment of ulcer. Dragstedt[26] in 1943 demonstrated the relation of the vagus nerve to ulcer formation. The psychogenic history in this case report emphasizes the significance of these findings.

Reported gastric ulcer in children prior to 1909 was consistently fatal. Although its incidence in children is not known, increasing evidence suggests that this symptom complex is more common than has previously been believed. Cases have been reported from many countries, the last occurring in Chile in 1950.[8] Autopsy findings on children dying from all causes list 0.1 to 0.2 per cent as having peptic ulcers.[27, 28] On this basis there may be approximately 50,000 children between one and six years of age who have subclinical gastric ulcer at the present time.

Figure 1 shows that 4 cases of gastric ulcer were reported in infants less than one year of age during the period 1909 to 1950, whereas 29 cases occurred in school-age children (seven to fourteen) and only 4 cases in the preschool group (age one to six). Line *xy* in Figure 1, extending from the infant group to the school-age group, bisects the preschool zone at 17. The expected accumulative incidence in preschool children from 1909 to 1950 should be approximately 17 cases instead of 4. Extending the trend line *xy* beyond the school child emphasizes the mounting incidence of ulcer in the adult population. The disparity in the reported attack rate in the preschool child is worthy of comment and suggests that this age group is neglected. A probable reason may be that infants under one year of age are frequently attended by the pediatrician or the family doctor, medical care thus being of better quality in this group. Likewise, in the school-age group (seven to fourteen years) the public-school nursing system provides adequate medical care. Thus the preschool child is left without controlled medical supervision.

The case report in this paper reflects the value of a detailed history. The family history of ulcer, the psychogenic background of the child, the onset and duration of symptoms and the presence of occult blood in the stool were diagnostic clues that suggested peptic ulcer and prompted early hospitalization and x-ray examination.

Table 1 presents abstracts from the histories of all reported cases of chronic gastric ulcer in the preschool child. In no case was the psychogenic pattern of the child discussed.

Summary

Forty-one cases of gastric ulcer in children have been reported in the literature since 1843. In the preschool child (age one to six years inclusive) gastric ulcer has occurred only 5 times (once prior to 1909, and 4 times since).

Before 1909 the diagnosis of gastric ulcer in children was made only at autopsy. Since then the mortality rate has dropped from 100 per cent to 8.5 per cent. At the same time the morbidity (in all age groups) has increased 900 per cent.

The incidence of subclinical gastric ulcers found at autopsy suggests a worldwide estimate at the present time of 50,000 cases in the age group of one to six years.

A report of a case of gastric ulcer in a five-year-old boy is presented. The clues for early diagnosis are discussed.

TABLE 1. *Recorded Cases of Gastric Ulcer in the Preschool Age, 1 to 6 Years.**

Author	Year	Sex	Age	Family History of Ulcer	Child's Personality Make-up	Bleeding	Perforation	Diagnosis	Therapy
			yr.						
Bechtold[30]	1904	F	5	Probable	Not mentioned		Yes	Autopsy	Medical
Loeber[3]	1929	F	3	Normal parents	Not mentioned	Yes	No	X-ray	
Burdick[29]	1940	F	6	Not mentioned	Not mentioned	Yes	No (?)	Autopsy	
Kraemer and Townsend[31]	1942	M	6	Uncle had duodenal ulcer	Not mentioned	Yes	No	X-ray	Medical
Martin and Saunders[9]	1948	M	6¼	Normal parents	Not mentioned	Yes	No	X-ray	Medical

*In many communities children enter school at 6 years of age.

Acknowledgment is given to Dr. Arthur M. Kimberly, consulting pediatrician at Memorial Hospital, and to the members of the X-Ray Department for their assistance in the study of this case.

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HYPOPOTASSEMIA IN UNTREATED DIABETIC COMA*

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WITH the development of acidosis in diabetic coma, fixed base, including potassium, is lost in large quantities. It is well known that despite this loss the initial serum potassium is usually normal or slightly elevated. In about 50 per cent of patients this depletion will be manifested by a fall in serum-potassium level within twelve to twenty-four hours after the start of therapy.[1-5] With the resumption of oral feeding, body potassium stores are usually replenished without difficulty. However, to depend on ordinary oral intake is dangerous and may be fatal. The following cases illustrate that the loss of potassium may be great enough to result in an initial low serum-potassium level, with clinical manifestations requiring the early administration of large amounts of potassium.

CASE REPORTS

A 22-year-old Negro woman entered the Los Angeles County Hospital on January 4, 1950, in coma. Her history, obtained from her parents, revealed that for 3 weeks she had been drinking large amounts of water, eating more than usual and urinating frequently day and night. There had been no vomiting or diarrhea. During this period she had lost an undetermined amount of weight and had rapidly become very weak. On the evening prior to entry the patient had complained of being "sick to her stomach" and in the morning was found in a semistuporous condition.

She had been well all her life, with no history of renal disease, hypertension or scarlet fever. However, in 1946 the development of pre-eclamptic toxemia in the 8th month of pregnancy required intervention by cesarean section. The baby was viable. Subsequent urinalysis and blood-pressure determinations were normal.

Physical examination on entry revealed a deeply comatose thin woman with Kussmaul respirations. Her blood pressure was 120/70. The eyeballs were very soft. The pupils were equal and regular and reacted to light. The fundi were normal. The neck was supple. The mucous membranes were dry. There was no cardiac enlargement, but a Grade I apical systolic murmur was heard. Auscultation and percussion of the chest revealed no abnormalities. Aside from a midline suprapubic scar, the abdomen was normal. All extremities were flaccid. Deep reflexes could not be elicited, and there were no pathologic toe signs. There was no response to painful stimulation.

Laboratory examination of the blood revealed a hemoglobin of 14 gm., with a hematocrit of 40, and a white-cell count of 27,000, with 95 per cent polymorphonuclear leukocytes. Urine sugar and acetone were ++++. Microscopical examination was negative. The specific gravity was 1.020. The plasma acetone was +++. The carbon-dioxide combining power was less than 4.4 milliequiv. per liter and the blood sugar 635 mg. per 100 cc. The nonprotein nitrogen was 55. Spinal-fluid examination revealed no abnormalities. The serum potassium was 2.3 milliequiv. per liter.

Immediately on entry the patient was given 40 units of crystalline zinc insulin intravenously and 40 units subcutaneously. A liter of one-sixth-molar sodium lactate was started. The stomach was washed with a 2 per cent solution of sodium bicarbonate, of which 200 cc. was left in. A Foley retention catheter was placed in the bladder. Three hours after entry, at 4:00 p.m., the patient's blood pressure had dropped to 85/50. One liter of plasma was immediately started. An electrocardiogram made at this time showed a normal sinus rhythm with a rate of 125. The PR interval was 0.12; the QRS interval was .08. The ST segments in Leads 1, 2 and 3 were slightly depressed, but the T waves were upright. The QT interval was 0.34. At 6:00 p.m., 5 hours after entry, the patient began to move about in bed and responded to stimulation. She had received 200 units of crystalline zinc insulin, including 80 units intravenously, 2 liters of one-sixth-molar sodium lactate with 2 gm. (27 milliequiv.) of potassium chloride and 1 liter of plasma. Her blood pressure had returned to its original level. At 7:00 a.m. on January 5, 18 hours after entry, she was still lethargic, but the deep reflexes were equal and active. The serum potassium was 1.8 milliequiv. per liter. By this time she had received 390 units of crystalline zinc insulin (including 100 intravenously) and 4 gm. (54 milliequiv.) of potassium chloride intravenously in a 0.1 per cent solution. The blood sugar was now 219 mg. per 100 cc. and the carbon dioxide was 25 milliequiv. per liter. Plasma acetone was negative. During the next 4 hours she received 1 liter of 5 per cent glucose in water and 1 liter of 5 per cent glucose in saline solution, with 1 gm. (13.5 milliequiv.) of potassium chloride in each liter. She was given 8 ounces of orange juice (containing about 500 mg., or 13 milliequiv., of potassium) by stomach tube. However, the patient was now again unresponsive to stimulation. The deep reflexes could not be elicited. Breathing was rapid and shallow, with all accessory muscles being used. The total urinary output to this time was 3200 cc. A lumbar puncture was again done, revealing a slightly xanthochromic fluid with normal dynamics. The electrocardiograph at this time revealed a rate of 140 per minute with a sinus rhythm. The PR interval was 0.14 and the QRS com-

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plex was .09 second. The ST segments in Leads 1, 2 and 3 were depressed. The T waves in Leads 1 and 2 were inverted; that in Lead 3 was flat. The T wave was upright in the first precordial lead but inverted in Leads CF 2 through 6. The ST segment was depressed in all precordial leads. The QT interval was 0.28 second.

The serum potassium determination just prior to death at 1:00 p.m. (24 hours after entry) was 1.07 milliequiv. per liter (4.2 mg. per 100 cc.).

Post-mortem examination revealed diabetes mellitus (clinical), hypopotassemia, a double renal pelvis and double ureter (left) and subarachnoid hemorrhage. The brain weighed 1120 gm. and was normal in appearance except for a very superficial subarachnoid hemorrhage over the right dorsolateral surface. Coronal sections revealed no gross lesions. The myocardium was a homogeneous reddish brown in color but showed yellow streaking and fatty infiltration at the base of the right ventricle. There were moderate atheromatous changes in the coronary arteries. The heart weighed 270 gm. The lungs showed no gross lesions. The pulmonary vessels were normal. The digestive tract was not remarkable except for several small submucosal gastric petechiae. The pancreas weighed 65 gm. and seemed to be fibrotic, with some distortion of the lobules. The liver weighed 1690 gm. The parenchyma was paler than normal, but the lobular markings were prominent.

The spleen weighed 100 gm. and was small and wrinkled in appearance. The tissue was reddish brown and soft, the malpighian bodies obscure. The left kidney weighed 140 gm., the right 160 gm. There was reduplication of the left ureter and renal pelvis. Both kidneys showed surface granulation, although the capsules stripped readily. There were a few areas of hemorrhagic streaking in the medullae.

Microscopical examination of the myocardium showed the muscle cells to be hazy in outline. There was a slight degree of perivascular fibrosis and increase in interstitial connective tissue. The pulmonary alveolar walls showed mild edema and congestion.

The renal glomeruli showed congestion but no hyaline changes. There was profound diffuse tubular cloudy swelling, with deposition of hemosiderin between the nuclei and basement membranes. Glycogen stain revealed finely granular light-pink deposits in the descending limbs of Henle's loop.

The parenchymal cells of the liver showed hydropic degeneration and vacuolization, especially about the central

TABLE 1. *Laboratory Data in Case 1.*

TIME	THERAPY			BLOOD				URINE		BLOOD PRESSURE	MISCELLANEOUS
	INTRAVENOUSLY GIVEN FLUIDS	INSULIN	CRYSTALLINE ZINC INSULIN	SUGAR	CARBON DIOXIDE	SERUM POTASSIUM	NON-PROTEIN NITROGEN	GLUCOSE	ACETONE		
				mg./100 cc.	*milliequiv./liter*	*milliequiv./liter*	*mg./100 cc.*				
1:00 p.m.	1000 cc. M/6 Na lactate	40	40	635	4.5	2.3	55	++++	++++	120/40	Hematocrit 40; plasma acetone +++; coma; Kussmaul respirations; 200 cc. $NaHCO_3$ left in stomach; absent deep reflexes.
4:00 p.m.	1000 cc. plasma 1000 cc. M/6 Na lactate 13 milliequiv. Kas KCl	40	40	629	4.5			++++	++++	85/50	ECG showed slight depression of ST segments and QT 0.34 (rate 125)
5:30 p.m.	1000 cc. M/6 Na lactate 13 milliequiv. K.		40					++++	++++	118/90	Patient began to respond to stimulation
7:00 p.m.		20	20	535	6.3			++++	++++		Plasma acetone +++
8:00 p.m.								++++	++++	138/70	Patient seemed more awake
10:00 p.m.			40	425	11.3			+++	++++	140/20	Plasma acetone ++++
1:00 a.m.	1000 cc. M/6 Na lactate 13 milliequiv. K			334				+++	++++	140/60	Patient asleep; deep reflexes elicited.
4:00 a.m.	1000 cc. 5% glucose in saline with 13 milliequiv. K		40		16.7			++	+++		Deep reflexes equal and active; patient lethargic but responded to stimulation.
7:00 a.m.	1000 cc. 5 per cent glucose in water with 13 milliequiv. K		30	219	24.3	1.8	48	++	+++	140/90	Plasma acetone negative; patient still lethargic.
9:00 a.m.	1000 cc. 5 per cent glucose in saline with 13 milliequiv. K.		40	250	24.3			++++	+++		Patient responded to stimulation; 8 ounces orange juice given by stomach tube.
11:00 a.m.	27 milliequiv. K in 1000 cc. 5 per cent glucose in water		20					++++	+++		Patient unresponsive; deep reflexes absent; breathing rapid and shallow with all accessory muscles used; ECG evidence of low potassium; lumbar puncture revealed xanthochromic fluid.
1:00 p.m.						1.07					Patient died

veins. There was an increase in interstitial fibrous tissue in the pancreas. The splenic pulp was congested and hemosiderin was present, both in free form and in macrophages.

CASE 2. Mrs. N. A., a 40-year-old Mexican woman, entered the Los Angeles County General Hospital in diabetic coma at 5:30 a.m. on November 14, 1950. Her diabetes had been discovered 3 years previously, when she complained of visual disturbances. She had been started on a diet and 30 units of protamine zinc insulin daily but controlled her diabetes poorly. She consulted her physician irregularly, indulged in dietary indiscretions and tested her urine infrequently. For the 5 months prior to admission she had taken no insulin and had lost 30 pounds. On November 11, 1950, she "sprained" her right ankle. This was followed by general malaise, vomiting and alternate periods of irrationality and stupor. The patient had had no treatment for the 3 days prior to entry into the hospital.

The patient was comatose on admission, with Kussmaul respirations and a strong acetone odor on her breath. The pulse was weak and regular. The temperature was 98.4°F. rectally. The blood pressure was 110/60. There was evidence of marked dehydration, the skin being dry and cool, the eyeballs soft, the tongue furrowed and brown and the rectum filled with hard impacted feces. The remainder of the physical examination was negative except for a right foot drop. The urinary bladder contained 500 cc. of urine.

Laboratory examination showed a ++++ urinary sugar, ++++ acetone, + albumin and occasional white and red blood cells; the blood sugar was 415 mg. per 100 cc., the carbon-dioxide combining power less than 4.4 milliequiv. per liter, the serum sodium 148 milliequiv. per liter, the chloride 119 milliequiv. per liter and the nonprotein nitrogen 29 mg. per 100 cc. The serum potassium was 3.3 milliequiv. per liter. The hemoglobin was 13.5 gm. and the white-cell count 19,000, with 72 per cent polymorphonuclear leukocytes.

On entry the patient was given 40 units of crystalline zinc insulin intravenously and 40 units subcutaneously. Fifteen hundred cc. of isotonic saline solution was administered intravenously over a 3-hour period. The stomach was gavaged with a solution of sodium bicarbonate. A blood for culture was drawn and penicillin started.

With treatment the patient became more responsive, and the Kussmaul respirations became less marked. At 8:30 a.m., 3 hours after the onset of treatment, however, it was noted that the patient was again comatose. Respirations were slow, shallow and irregular, with dilatation of the alae nasi and "fish-mouth" gasping. The blood pressure had fallen to 94/60. An electrocardiogram showed a rate of 75, a PR interval of 0.14, a QRS complex of 0.07, sagging ST segments and biphasic T waves in all leads, with a QT interval of 0.56 (Fig. 1*A*). Examination of the blood revealed a sugar of 379 mg. per 100 cc., a carbon dioxide still less than 4.4 milliequiv. per liter, a ++++ urinary sugar and ++++ acetone. A diagnosis of hypokalemia was made; 2 gm. (27 milliequiv.) of potassium chloride was administered rapidly in 500 cc. of normal saline solution and 8 gm. (108 milliequiv.) of a 10 per cent solution was given intragastrically by Levine tube. Five hundred cc. of plasma was given intravenously, 40 units of crystalline insulin subcutaneously. By 9:30 a.m. the patient had reacted with reappearance of Kussmaul respirations and responded to touch and voice, and the blood pressure had risen to 112/60. One liter of 5 per cent glucose in saline solution with 3 gm. (40 milliequiv.) of potassium chloride was administered.

At 10:30 a.m. the blood sugar was 385 mg. per 100 cc., the carbon dioxide still less than 4.4 milliequiv. per liter, and

TABLE 2. *Laboratory Data in Case 2.*

TIME	THERAPY			BLOOD				URINE		BLOOD PRESSURE	MISCELLANEOUS
	INTRAVENOUSLY GIVEN FLUIDS	INSULIN	CRYSTALLINE ZINC INSULIN	SUGAR	CARBON DIOXIDE	SERUM POTASSIUM	NONPROTEIN NITROGEN	GLUCOSE	ACETONE		
				mg./100 cc.	*milliequiv./liter*	*milliequiv./liter*	*mg./100 cc.*				
11-14-'50											
5:30 a.m.	1500 cc. saline	40	40	415	4.5	3.3	29	++++	++++	110/60	Patient in coma
6:30 a.m.								++++	++++	120/70	Patient responsive
7:30 a.m.								++++	++++	120/70	
8:30 a.m.	500 cc. saline with 27 milliequiv. K, 500 cc. plasma (108 milliequiv. K by gavage)		40	379	4.5			++++	++++	94/60	Patient comatose; shallow respirations. ECG; low serum potassium.
9:30 a.m.	1000 cc. 5 per cent glucose in saline with 40 milliequiv. K							++++	++++	112/60	Patient again responsive; Kussmaul respirations reappeared.
10:30 a.m.			40	385	4.5	3.0		++++	++++	120/70	
12:00 m.	1000 cc. 5 per cent glucose M/6 Na lactate with 27 milliequiv. K		35					++++	++++		
1:40 p.m.	2000 cc. 5 per cent glucose in saline, 54 milliequiv. K		35	645	8.6			++++	++++	134/70	
4:00 p.m.			35					++++	+++		
4:30 p.m.				660	10.0			++++	+++		
5:30 p.m.								++++	++		Patient awake, weak; ECG unchanged; 6 oz. of orange juice with 81 milliequiv. K.
10:00 p.m.	1000 cc. 5 per cent glucose with 13 milliequiv. K		40	480	16.8			++++	+		
11-15-'50											
2:00 a.m.								++++	0		
6:00 a.m.	1000 cc. 5 per cent glucose		30					++++	0		Liquid diet started
8:00 a.m.				300	20.0	5.6		++++	0		ECG returned to normal

the serum potassium (subsequently reported) 3 milliequiv. per liter. Forty units of insulin was given. An electrocardiogram at 10:55 a.m. showed little change.

At 12:00 noon, after 6½ hours of therapy, the urine showed ++++ sugar and ++++ acetone. Thirty-five units of insulin and 1 liter of 5 per cent glucose in one-sixth-molar sodium lactate were given. At 1:40 p.m., the blood sugar was 645 mg. per 100 cc. and the carbon dioxide had risen to 8.6 milliequiv. per liter. Thirty-five units of insulin and 1 liter of 5 per cent glucose in saline solution with 2 gm. (27 milliequiv.) of potassium chloride were given. At 2:40 p.m. the last liter of fluid was repeated. At 4:00 p.m. the urine sugar was ++++, but the acetone had fallen to +++.

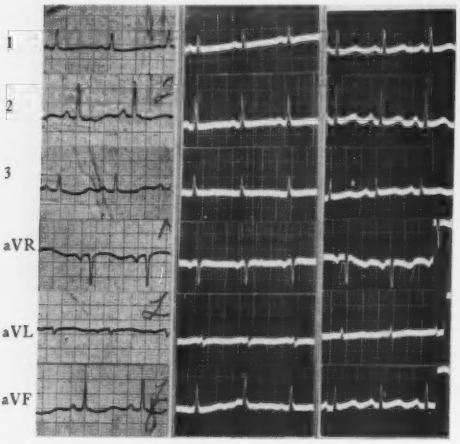

FIGURE 1. *Electrocardiograms in Case 2.*
A *and* B = *Typical electrocardiographic changes of hypopotassemia.* C = *Return to normal with therapy.*

Thirty-five units of insulin was given. At 4:30 p.m. the blood sugar was 660 mg. per 100 cc., the carbon dioxide 10 milliequiv. per liter and the total urinary output 3250 cc.

Although by 5:30 p.m. (12 hours after entry) the patient was greatly improved, she was still apathetic and weak. Another electrocardiogram at this time showed no change. Therefore 6 ounces of orange juice and 6 gm. (81 milliequiv.) of potassium chloride were given orally. By this time the patient had received more than 25 gm. (337 milliequiv.) of potassium chloride. The urine showed ++++ sugar and ++ acetone. At 10:00 p.m. the blood sugar was 480 mg. per 100 cc. and the carbon dioxide 16.8 milliequiv. per liter. Forty units of insulin was given subcutaneously with 1 liter of 5 per cent glucose in water containing 1 gm. of potassium chloride intravenously. At 2:00 a.m. of the next day, November 15, the urine finally showed no acetone but still had ++++ sugar. The total urinary output was now over 7 liters; the patient was receiving her 8th liter of intravenously given fluids and had had 305 units of crystalline insulin.

At 6:00 a.m. 30 units of insulin and 1 liter of 5 per cent glucose in water were given. A liquid diet was started. Examination of the blood at 8:00 a.m. showed that the serum potassium was 5.6 milliequiv., the chloride 135 milliequiv., the serum sodium 161 milliequiv. per liter, the blood sugar 300 mg. per 100 cc., and the carbon dioxide 20 milliequiv. per liter. An electrocardiogram still showed low T waves, but the ST segments were no longer depressed (Fig. 1*B*).

Improvement continued steadily. The orthopedic consultant constructed a posterior molded splint for the right leg and instructed the patient in passive and active exercises. An ophthalmologist confirmed the presence of an inactive retinitis proliferans.

The patient was discharged on December 1 on 45 units of protamine zinc insulin and a restricted diet. An electrocardiogram on this date was normal (Fig. 1*C*).

DISCUSSION

Whereas most patients in diabetic coma have serum-potassium levels that are normal or slightly elevated on entry,[1] those two cases were unusual in that both showed low initial values. In any diabetic coma, with the development of acidosis, glucose and keto-acids are excreted in large quantities, carrying with them fixed base, including potassium. Vomiting and diarrhea result in further loss. Butler[6, 7] has estimated a total loss of 6 milliequiv. of potassium per kg. of body weight in diabetics with pre-coma acidosis, nausea and an added day of vomiting during withdrawal of insulin for three to four days, half of which cannot be accounted for by tissue catabolism on the basis of nitrogen loss. With the associated inadequate food intake, little or no potassium is obtained. Thus, with the operation of all these factors, the body stores of potassium are depleted, the extent of the depletion depending on the severity and duration of the pre-coma period.

The initial serum-potassium level, not a true indication of the total body potassium, depends on additional factors. Dehydration, with contraction of the plasma and extracellular volumes, increases serum-potassium concentration. Extracellular and cellular dehydration are also conducive to the migration of potassium from cells. Starvation and tissue breakdown release protein-bound potassium. Interruption of carbohydrate metabolism in vitro in red blood cells is associated with liberation of potassium, as is glycogenolysis in the liver.[8] Impaired renal function may also be a contributory factor.[1] Therefore it is apparent that the serum potassium level at a given time will vary according to the factors predominating. In contrast to most cases of diabetic coma, dehydration and tissue breakdown were insufficient to mask the severe depletion of total body potassium as measured by serum-potassium levels present in both these patients.

With the beginning of treatment, the serum-potassium concentration falls as the extracellular fluid space expands, carbohydrate metabolism and glycogenesis are resumed in the liver and muscles, tissue protein is deposited and renal function improves. Intravenously given fluids, especially saline solution, cause further depletion of body potassium through loss in the urine.[1, 4] With the administration of large amounts of potassium-free fluids and insulin as advocated by some authors,[9] the serum potassium may fall abruptly to a level low enough to cause respiratory paralysis and cardiac damage. This therapy is especially dangerous if the initial value is low, as illustrated in the

cases above. Possibly both these patients should have received more insulin earlier. With the low serum-potassium levels on entry, however, intensive therapy of this sort without potassium might have resulted in a more precipitous drop in serum potassium. Since serum-potassium determinations are usually not immediately available in most institutions, — and even early feeding of liquids and foods containing potassium may be inadequate, — the intravenous administration of potassium must be considered.

The cases presented serve to emphasize the importance of the routine parenteral use of potassium as advocated by some workers[1, 6, 7, 10, 11] early in the treatment of diabetic coma after hydration has started, provided that urinary output is adequate. Potassium therapy must be extremely vigorous if a fatal outcome is to be avoided in cases such as these, in which total body potassium has apparently been greatly diminished.

The electrocardiogram is thought to be a fairly reliable index of qualitative but not quantitative changes in serum potassium and can be used to follow a patient's course during treatment.[11-13] Adequate potassium therapy for the uncomplicated case appears to be that suggested by Martin.[14] Two to 4 gm. (27-54 milliequiv.) of potassium chloride as a 0.1 to 0.2 per cent solution are given in the second to fourth hour after insulin has been given and hydration started. If urinary output is satisfactory, potassium is added to each subsequent liter of fluid, and in addition 2 gm. (27 milliequiv.) is given orally every four hours.

Summary

Two patients in diabetic coma are described, with low serum-potassium levels on entry and clinical manifestations of hypokalemia.

Early and adequate parenteral potassium administration in the routine treatment of diabetic coma is suggested.

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MEDICAL PROGRESS

ELECTROLYTE AND FLUID DISTURBANCES IN CONGESTIVE HEART FAILURE (Concluded)*

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EFFECT OF SODIUM-CHLORIDE INGESTION IN HEART FAILURE

Studies to determine whether cardiac edema followed a primary retention of sodium and water or was first preceded by an elevation in venous pressure were made by administering 10 gm. of sodium chloride daily to patients previously treated for heart failure. Such studies were reported to show the recurrence of cardiac edema, as denoted by weight gain, before the venous pressure became elevated.[97] Later studies were ineffective in determining such a sequence, both gain in weight and elevation of venous pressure occurring virtually at the same time.[98, 99]

In interpreting such studies it is important to recognize that in most cases of congestive heart failure, failure of the left side of the heart and pulmonary congestion precede failure of the right side of the heart. In two cases in which I administered 10 gm. daily of sodium chloride after the patients had largely recovered from heart failure, I observed that gain in weight preceded a rise in peripheral venous pressure. However, this gain in weight was accompanied by increasing orthopnea, intensification of the second pulmonic sound, reduction of vital capacity and prolongation in circulation time, although the systemic venous pressure had not yet become elevated. Thus the weight gain could be due to a congestion localized in the pulmonary circulation and to an increase in pulmonary interstitial fluid, and this in turn could denote an increase in pulmonary venocapillary hydrostatic pressure, which could not be measured directly. The weight gain could then be related not only to sodium-water retention but also to increased venous pressure, the latter only in the pulmonary circulation. The question of precedence of sodium-water retention and venous pressure would still remain unanswered.

On the other hand, when digitalis is withdrawn from a patient under satisfactory treatment for heart failure (that is, on a low sodium intake), the venous pressure rises without an accompanying gain in weight.[99, 100] Because of this difference, it has been suggested that there may be two types of congestive heart failure, one due to sodium-water retention and characterized chiefly by edema and gain in weight, with elevation of venous pressure but no dyspnea and controlled by mercurial diuretics, and a second characterized chiefly by a rise in venous pressure and dyspnea and controlled by digitalis but not by mercurial diuretics.

These are not different forms of heart failure but variations of the clinical picture, depending on whether or not the manifestations resulting from sodium-water retention are prevented by strict avoidance of sodium ingestion. When digitalis is withdrawn from a patient with heart failure whose edema has been eliminated and who is receiving a minimal quantity of sodium there is a further deterioration of cardiac function, resulting in a reduction of an already inadequate cardiac output. This may lead to a prompt elevation of venous pressure because the undigitalized, deficient heart can no longer properly accept and eject the venous return. On the other hand, edema may not occur because the sodium-water retention necessary to its formation is artificially inhibited by the low sodium intake.

The response of the patient with heart failure to the ingestion of sodium chloride may be considered from another viewpoint:

An average diet containing 10 gm. of salt can be handled satisfactorily by a normal person; that is, there will be no abnormal accumulation of sodium and water. On the other hand, a patient with heart failure will excrete most of the ingested salt, but some will be retained. In due time the manifestations of heart failure, including edema, will become apparent or will be accentuated. If 25 gm. instead of 10 gm. of sodium chloride daily is given to a normal person, not all of it will be excreted promptly. If continued for more than a few days, the extracellular fluid will increase,[101] and eventually the increase in extracellular fluid is manifested by visible edema. Thus 10 gm. daily of sodium chloride will usually produce edema in the patient with heart failure, whereas 25 gm. daily will be necessary to cause edema in the normal person. The situation is somewhat analogous to the occurrence of dyspnea on exertion in the patient with heart failure or in the normal person. In the former, a slow walk may cause breathlessness; in the latter, dyspnea occurs only after exertion requiring speed or endurance beyond the range of ordinary activity. In heart failure there is a diminished tolerance of sodium intake, as there is a diminished tolerance to

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physical exertion. However, sodium intake and physical exertion are not in themselves responsible for the syndrome of heart failure; they are stresses that produce or intensify symptoms in hearts that have already failed.

Mechanism of Sodium-Water Retention in Heart Failure

It has long been apparent that the hypervolemia, edema and other features of heart failure could not develop and persist unless the kidney failed to excrete as much salt and water as the patient ingested. Many studies have demonstrated that when large quantities of sodium chloride are administered orally or by vein to patients with congestive heart failure the renal excretion of this salt and of water is distinctly less than in normal persons.[102, 103] It has also been observed that administration of the chloride ion in the form of ammonium chloride does not cause a retention of salt and water and in fact produces a diuresis.[104, 105] These and similar observations have indicated that a deficiency in sodium excretion is the important renal factor in the fluid retention of congestive heart failure.[106] The renal deficiency in sodium excretion in cases of heart failure is relative. Increased intake of sodium chloride usually augments excretion of this salt, but the response is less than in the normal; consequently the patient retains more than he excretes.

There is still uncertainty concerning the mechanism responsible for sodium and water retention in heart failure as well as concerning the stimulus initiating this mechanism. This is due in part to lack of knowledge of the factors regulating renal excretion of sodium and water in the normal person. The mechanisms responsible for abnormal renal retention of sodium and water will be discussed under the headings "intrinsic renal factors," "adrenal-cortical hormones," "other hormones" and "cellular factors."

Intrinsic Renal Factors in Heart Failure

Diminished Glomerular Filtration

Recent studies with the aid of cardiac catheterization have demonstrated anew that in congestive heart failure the cardiac output is diminished; they have also disclosed that the renal blood flow is diminished to an even greater degree.[82] Glomerular filtration is substantially reduced.[94, 95] If the percentage of tubular reabsorption of sodium is regarded as being constant, the diminished renal excretion of sodium may then be attributed exclusively to the reduction in glomerular filtration.

Several objections have been raised to the explanation of abnormal renal retention of sodium in heart failure by a reduction in glomerular filtration. The glomerular filtration may still be low even after the patient has "recovered" from heart failure.[71, 94, 107-109] In cases of glomerulonephritis the glomerular-filtration rate is low, but edema is often absent. However, sodium retention in heart failure is considered to depend on diminished glomerular filtration because tubular reabsorption is at least normal, if not increased; in other words, there is a glomerulotubular imbalance. In glomerulonephritis tubular as well as glomerular function is diminished. Hence, abnormal sodium retention need not follow a reduction in glomerular filtration, because this is neutralized by at least an equal reduction in tubular reabsorption of sodium.

Increased Tubular Reabsorption

Abnormal renal excretion of sodium in heart failure may be due to increased tubular reabsorption.[96, 110] This is suggested by our knowledge that the tubules are important in the regulation of sodium metabolism in the normal person, especially in maintaining the acid-base balance, isotonicity and volume of body fluids. Actual measurements of tubular reabsorption by present methods are insufficiently exact to determine whether this is unchanged or increased in heart failure, for if 99½ per cent instead of 99 per cent of the daily 180 liters of glomerular filtrate were reabsorbed, 0.9 liters instead of 1.8 liters of urine would be excreted; that is, the excretion of urine (and sodium) would be halved.

If tubular reabsorption of sodium is increased in heart failure, it remains to be determined whether and to what degree this is secondary to the diminished glomerular filtration, to adrenal cortical stimulation or to local renal tubular factors. A more exact understanding of local renal tubular mechanisms is desirable. It is apparent that the tubule cells perform work in reabsorbing electrolytes and other substances against the pressure gradient between the tubular luminal contents and the tubular interstitial tissue. Specific tubular activity is involved in the conservation of sodium. Carbonic-acid anhydrase and other enzymes are undoubtedly concerned in this tubular transport of sodium, but there is uncertainty concerning the exact mechanisms. The possibility has been suggested that the tubule cells act as cation-exchange resins that yield hydrogen, ammonium or potassium ions in exchange for sodium.[111, 112] Whether or not heart failure directly or indirectly modifies the ionic and enzyme reactions of the tubule cells, resulting in excessive sodium retention, is undetermined.

Increased Renal Venous Pressure

Increase in renal venous pressure is still another mechanism considered responsible for the diminished renal excretion of sodium in heart failure.[83, 113] In the experimental production of constrictive pericarditis, a reduction in renal output of water and sodium is associated with a rise in venous pressure, even though resting cardiac output, renal blood flow and glomerular filtration are at control levels.[114] An elevated venous pressure has been found in the

renal vein of patients with congestive heart failure.[114] Partial occlusion of one renal vein in dogs caused a diminution in sodium and water excretion only from the kidney subjected to an increased renal venous pressure.[113] These disturbances in sodium excretion seemed to be independent of any changes in glomerular filtration or renal blood flow. It seems apparent that increased renal venous pressure is one of the mechanisms capable of reducing renal excretion of sodium, just as diminished glomerular filtration or increased tubular reabsorption is similarly capable. However, it is improbable that increased renal venous pressure is the actual mechanism responsible for increased renal retention of sodium in patients with congestive heart failure. Certainly, in many if not in most patients, deficient sodium excretion is already present in the early stages of heart failure when failure is limited to the left side and when the venous pressure in the systemic circulation including the renal vein is not elevated. Furthermore, the renal inefficiency in excreting sodium persists even after the venous pressure has been reduced to normal with the aid of mercurial diuretics and restriction of sodium.

Adrenal Cortical Hormones

The adrenal cortex has been assigned a primary role in the regulation of sodium and water. In normal persons a diminished sodium intake is followed by a reduction in the renal excretion of sodium. In the absence of the adrenal cortex, as, for instance, in Addisonian crisis, the renal excretion of sodium is excessive despite a diminished sodium intake.[116, 117] This suggests that the adrenal cortical secretion affects sodium excretion by its action on the tubules (that is, diminished reabsorption), since the glomerular filtration and the filtration fraction are diminished[118, 119] although the excretion of sodium is increased. The synthetic adrenal cortical hormone desoxycorticosterone is a powerful sodium-water retaining factor.[120] To a much lesser extent pituitary adrenocorticotrophic hormone (ACTH) and the adrenal cortical hormone cortisone cause an early renal retention of sodium[121-123] despite the fact that there is a rise in glomerular filtration.[124] When the sodium intake is not sharply restricted, these adrenocortical hormones may cause edema, including pulmonary edema. Furthermore, such accumulation of excessive water is accompanied by many of the dynamic disturbances in pressure and flow usually found in congestive heart failure.[125]

In the normal person, sodium-chloride depletion or loading results in diminished or increased excretion of sodium chloride, respectively. Leaf and Couter[126] have presented evidence that such renal sodium excretion in the normal person is regulated by adrenal cortical activity and that the rate of secretion of the adrenal cortical hormone varies inversely with the salt load. In other words, a low sodium intake stimulated adrenal cortical activity with secretion of a DOCA-like hormone that caused renal conservation of sodium. Insofar as this mechanism operates in patients with congestive heart failure, it tends to neutralize the benefit of a low-sodium diet.

Although there is definite evidence that adrenocortical hormones can produce retention of sodium and water, the evidence that it is an actual factor in the renal retention of sodium and water in congestive heart failure is only suggestive. An increased amount of urinary corticoids[127] and desoxycorticosterone-like material[128] has been observed in patients with congestive heart failure. The reduction of sodium output in the sweat,[129] the saliva,[130] and the urine of patients with congestive heart failure has been attributed to increased adrenocortical activity in such patients. Furthermore, these observations suggest a widespread and perhaps primary adrenocortical effect in heart failure, rather than a limited influence on the renal tubules.

Antidiuretic and Other Hormones

In congestive heart failure we are particularly interested in the elimination of excessive water. However, the basic disturbance is a deficient excretion of sodium, and actually elimination of the excessive fluid can be accomplished only by elimination of the excessive sodium. Hypophysectomy does not prevent the renal conservation of sodium or excretion of potassium.[131] The antidiuretic hormone (ADH) of the posterior lobe of the pituitary gland has no effect on the excretion of sodium chloride. Although it tends to cause renal retention of water and produce a more concentrated urine of diminished volume, the absolute quantity of sodium in the urine is unchanged.[132]

There is a dissociation between the quantity of sodium and water absorbed in the distal tubule. This is attributed chiefly to pituitary antidiuretic hormone (ADH), which acts on the distal tubule to inhibit the excretion of water without directly affecting that of sodium.[133] The maximal inhibitory effect of ADH on water excretion is limited by an obligatory need of water to excrete various solutes.[134] On the other hand, in the absence of ADH (as in diabetes insipidus) 15 to 20 liters of urine may be passed daily, representing most of the glomerular filtrate that reaches the distal tubule. Nevertheless, sodium depletion does not occur.

Because of these considerations ADH is not regarded as a primary factor in the accumulation of excessive fluid in congestive heart failure. The finding of antidiuretic hormone in the urine in states associated with salt retention and edema, such as cirrhosis of the liver[135] and congestive heart failure,[136] does not denote that this is an important initiating factor in the formation of edema. When present, it may represent a secondary consequence of disturbances in fluid and electrolytes previously caused by disease of the liver or failure of the heart.

The excretion of posterior-pituitary antidiuretic hormone appears to be stimulated by an increase in effective total osmotic pressure of the blood supplied to it by the internal carotid artery.[137, 138] However, other stimuli, emotional or neurogenic, arising from the hypothalamus or other cerebral centers may have a similar effect.[139] In congestive heart failure the osmotic pressure of the blood is normal or diminished; hence one would anticipate no increase or a reduction in ADH. However, other mechanisms may be invoked in heart failure that stimulate the production of this hormone.

Other hormones and humoral agents have been implicated as possible factors in the diminished renal excretion of sodium and water. Vasoexcitor material (VEM)[140] and renin[82, 141] have been reported as present in the renal venous blood of patients with congestive heart failure, and vasodepressor material (VDM) has been found in the hepatic venous blood.[140] Testosterone and progesterone have sodium-water retaining effects,[142, 143] but the mechanism of their action is uncertain, and there is no evidence that they contribute to the formation of cardiac edema.

Cellular Disturbances in Heart Failure

The fall in cardiac output that occurs with heart failure affects all the other tissues and organs, as well as the kidney. Therefore, the stimulus to sodium and water retention may be initiated by changes in any or many of these sites. The effect on individual organs such as the kidney, the adrenal gland, the pituitary gland and the liver has already been indicated. Widespread disturbance with the various cells of other tissues may occur when the blood flow becomes inadequate. The suggestive though inconclusive evidence that potassium leaves the cells during heart failure and returns after recovery has been mentioned. Changes in cellular metabolism may lead to an increase in water content within the cell and to diminished osmotic pressure or to dehydration of the cell with consequent hyperosmolarity. It has been suggested that such alterations in cellular osmolarity may initiate the renal mechanisms leading to disturbances in electrolyte and water retention.[144, 145] Loss of intracellular potassium in heart failure might affect renal sodium excretion by concomitant changes in intracellular osmolarity or by other mechanisms. It is well to recall the converse behavior of sodium and potassium with respect to renal excretion, under various circumstances. The kidney appears especially equipped to conserve sodium and to excrete potassium. Potassium is retained when sodium is abnormally excreted in hypoadrenal states,[116, 146] whereas sodium is retained and potassium is abnormally excreted in hyperadrenal states and during administration of adrenal cortical hormones.[123, 147]

The Relation of Renal Retention of Sodium in Congestive Heart Failure to Various Homeostatic Mechanisms

The mechanism responsible for the abnormal renal excretion of sodium in congestive heart failure may be considered from the viewpoint of the renal function in maintaining homeostasis. The kidney is the effector organ in several mechanisms designed to preserve the constancy of the pH of the blood and other body fluids, the constancy of the osmotic pressure of the extracellular fluid and the constancy of the plasma and extracellular volume. One may speculate concerning whether the abnormal retention of sodium and water in heart failure results from an unusual and constant stimulus that serves to preserve or restore these constants or from a stimulus serving to restore some other important homeostatic constant.

Regulation of Blood pH

Normally the kidney aids in maintaining the blood pH at a constant level of about 7.4. Conservation of sodium is an important feature in this regulatory function of the kidney.[111, 148, 149] In congestive heart failure the normal pH of the blood is usually maintained, and the renal function of conserving sodium is not only preserved but exaggerated. Is this because heart failure presents an intense and chronic threat of acidosis? The diminished blood flow in heart failure might be expected to induce tissue anoxia and increased acidic metabolites. These, in turn, might be regarded as an increased stimulus to sodium retention. However, the hypoxia of chronic pulmonary disease is not associated with sodium retention and edema, and experimental hypoxia due to breathing low concentrations of oxygen does *not* reduce glomerular filtration and tends to *increase* sodium excretion.[150, 151] These observations suggest that hypoxia per se is not responsible for the abnormal renal excretion of sodium observed in congestive heart failure, although the experimental conditions do not exactly duplicate those associated with the hypoxia of deficient cardiac output.

Regulation of Osmotic Pressure

In the normal person an increase in total osmotic pressure due to excess of sodium results in stimulation of the posterior pituitary gland, with increased excretion of ADH. The ADH causes retention of water, which, together with increased water ingestion due to thirst, restores the normal osmotic pressure of the extracellular fluid. Conversely, a low osmotic pressure due to diminished concentration of sodium in the extracellular fluid inhibits pituitary secretion of ADH and tends to increase the renal excretion of water. If this mechanism operates also in congestive heart failure, it is a major paradox that although the extracellular concentration of

sodium is low or normal[37, 38] there is a persistent retention of water by the kidney even when this renders the extracellular fluid hypotonic.

Regulation of Plasma and Extracellular Volume

The function of the kidney in maintaining a normal plasma and extracellular volume is also closely related to its handling of sodium and water. In the normal person a *reduction* in plasma or extracellular volume leads to diminished excretion of sodium, that is, to sodium retention. Presumably this then stimulates additional secretion of ADH, with consequent retention of water and restoration of extracellular volume. Conversely, an increase in plasma and extracellular volume, such as follows infusions of isotonic sodium chloride, augments the excretion of sodium and water. The diminution and increase in sodium excretion, with resultant diminution and increase in extracellular fluid volume, has been related to corresponding depression or elevation in the rate of glomerular filtration.[162] In this mechanism congestive heart failure presents a second major paradox, for there is a persistent tendency toward sodium retention in spite of a large increase in plasma and extracellular volume. In other words, the abnormal retention of sodium in heart failure is not induced, as in the normal person, by an absolute deficiency in extracellular volume.

Regulation of Cardiac Output

It is appropriate to recall at this point that under severe stress homeostasis cannot always be maintained. There is apparently an order of importance of the different constants; at least some of these constants are disturbed more readily than others. The mechanisms designed to maintain homeostasis with respect to these different elements often conflict; hence one constant may be retained at the expense of another. The constancy of extracellular volume is upset more readily than that of osmotic pressure, and the latter is altered more readily than the pH.

Like the pH of the blood, the osmotic pressure of the plasma and the plasma and extracellular volume, the cardiac output may also be regarded as a relative "constant" that several mechanisms serve to maintain. Cardiac dilatation and hypertrophy can long preserve a normal cardiac output despite the handicap of chronic hypertension, valvular or myocardial disease. Likewise renal retention of sodium (and consequently of water) appears to follow the physiologic or pathologic stresses that tend to diminish the cardiac output or that tend to render the basal cardiac output inadequate. The upright position results in a retention of sodium[152-155] that can be correlated with a reduction in the venous return and therefore in the cardiac output. Sodium retention during exercise[71, 156] may be similarly related, for although the absolute cardiac output is increased there is a temporary deficiency with respect to the needs of the tissues. The retention of sodium during exercise is independent of changes in filtration rate as measured by the inulin-clearance method or endogenous creatinine.[71] Sodium retention by the kidney following hemorrhage[157] and various shock states[158] is associated with a sharp reduction in the cardiac output. In all these instances the retention of sodium (and secondarily of water) may be regarded as a vital compensatory mechanism that tends to restore an adequate cardiac output. Increase in plasma volume due to sodium-water retention serves to accomplish this end.

In congestive heart failure there is an absolute or relative deficiency in cardiac output, with sodium and water retention and increase in plasma volume. Whether the latter is teleologically designed to restore cardiac output and whether it actually does so are unanswered questions. Cardiac failure is denoted by a fall in cardiac output, diminished cardiac emptying and a rise in venous pressure. The latter results in transudation of fluid and a reduction in plasma volume, which serves to reduce further the cardiac output. Early retention of sodium and water tends to restore a normal plasma volume. However, mere restoration of a normal plasma volume does not suffice to compensate the deficient cardiac output. The process of sodium retention persists as long as an inadequate cardiac output has not been or cannot be restored. As with other compensatory mechanisms, sodium and water retention with consequent accumulation of plasma and interstitial fluid may overshoot the ideal objective and result in symptoms without restoring cardiac output. A partial reduction in plasma volume, as by diuretics or phlebotomy, may actually be of benefit, but efforts to reduce the extracellular or plasma volume to normal may produce equally unpleasant or dangerous symptoms of a deficient cardiac output.

Some of the inconsistencies or paradoxes of sodium and water retention in congestive heart failure may be explained if maintenance of a normal cardiac output is regarded as one of the renal homeostatic objectives. Furthermore, it should be recognized that under severe stress or disease the mechanisms maintaining the various homeostatic objectives may conflict with each other. In the presence of a high plasma and extracellular volume the normal renal response should be an increased excretion of sodium and water, which would serve to restore a normal extracellular volume. However, in heart failure this mechanism apparently conflicts with the more dominant stimulus to retain sodium and water, possibly to restore the inadequate cardiac output.

Fluids, Electrolytes and the Treatment of Heart Failure

The impact of recent studies in fluids and electrolytes has led to certain changes in our treatment of congestive heart failure:

Recognition of the important role of sodium and water accumulation in producing the symptoms of heart failure, and the dramatic improvement that follows diuresis due to mercurial diuretics and salt restriction, have relegated the treatment of the heart itself to a secondary position. Less emphasis is now placed on the importance of bed rest or of restricting activity or on careful and continued digitalization than on control of sodium and water. There should be no question of a competitive choice between sodium and water regulation or rest and digitalization. Both should be carried out with equal diligence. Although more dramatic symptomatic results are usually obtained through mercurial diuretics and sodium restriction, these measures represent only symptomatic treatment. It is probable that as we improve surgical and medical ability to control hypertension, valvular defects, coronary-artery disease or myocardial disturbances the pendulum of our therapeutic emphasis will shift to a more direct approach to the basic causes responsible for failure of the heart.

Fluid restriction to 1000 cc. or less daily, generally recommended in the treatment of heart failure only ten years ago, is no longer advocated. The primary importance of restricting sodium is generally acknowledged and the intake of fluids has been greatly liberalized, but the belief that very large intakes of fluid (5 liters of water or more daily) should be given to promote diuresis has not gained widespread acceptance.[159] However, there is evidence that in the absence of extreme environmental temperatures the optimal fluid intake is between 2000 and 3000 cc.[160]

The desirability of restricting the intake of salt in the treatment of heart failure has been known for some fifty years. Recent advances concern the degree of sodium restriction that is necessary for effective therapy. It is probable that the sodium tolerance of patients with heart failure varies considerably. However, it has become apparent that many such patients will not respond to treatment unless the restriction of sodium intake is far more severe than was formerly recommended. Elimination of the salt shaker, — even the banning of salt in cooking, — rarely reduces the daily sodium-chloride intake to below 2 or 3 gm. The Karrell diet, permitting 800 cc. of whole milk daily but no other food, contains 1.2 gm. of sodium chloride. This low sodium content accounted for its frequent effectiveness when other seemingly salt-restricted diets had failed. On the other hand, the Karrell diet may also be ineffective, for there are patients with congestive heart failure who do not lose their edema unless the daily sodium-chloride intake is less than 500 mg. (that is, unless their sodium intake is less than 200 mg. daily). The importance of such intense sodium restriction has led to a more widespread knowledge of the sodium content of various foods, and particularly to the relatively high sodium content of such staple foods as breadstuffs, milk, cheese, eggs and meats. This, in turn, has led to the manufacture of salt-free bread, dialyzed milks and high-protein, high-caloric, low-sodium milk powders. Furthermore, the need for careful checking of the patient's sodium intake has resulted in more systematic analysis of the urine for sodium, a procedure that has been facilitated by the development of a practical means of sodium analysis with the aid of the flame photometer.

The use of ion-exchange resins is becoming more widespread as a corollary to the need for severe sodium restriction and the consequent unpalatability of the diets.[161-164] These resins are insoluble and nonabsorbable polymers containing large molecules with ions that can move freely out of the solid in exchange for other ions. The resins used in the treatment of heart failure have hitherto been cation resins, carboxylic compounds containing positive ammonium or hydrogen ions capable of removing sodium, potassium, calcium and magnesium from solution. The hydrogen or ammonium is released in part into the intestinal tract in exchange for sodium and other cations, which are then eliminated in the feces with the nonabsorbed resin. Thus a substantial proportion of the dietary intake of sodium is never absorbed. However, potassium is likewise removed, and unless it is adequately supplemented by the ingestion of potassium salts, hypokalemia may result. Therefore cation resins now available contain 1 part potassium to 2 or 3 parts hydrogen or ammonium, which prevents potassium depletion. Another difficulty in the use of these resins is the development of acidosis due to the absorption of ammonium chloride or hydrochloric acid, which is formed when the ammonium or hydrogen from the resin combines with the chloride in the intestinal tract. Because of the danger of acidosis, the resins are contraindicated in patients with renal insufficiency, especially when there is a deficiency in the renal production of ammonia necessary to control acid-base balance.[165] To avoid acidosis, resins are now available that contain anion-exchange resin (with replaceable hydroxyl ions) in addition to the hydrogen-potassium cation resin.[166] The hydroxyl ions are released and combine with and neutralize the hydrogen ions released from the cation-exchange resin, thus preventing acidosis. Unpalatability, constipation and other gastrointestinal symptoms associated with the ingestion of the earlier available exchange resins are currently being corrected. Sodium restriction is still essential despite the use of resins, but the latter permit enough freedom in the ingestion of sodium-containing foods to make the diet palatable and hence to enable the patient to adhere to the necessary dietary restriction. The ideal dosages of the resins have not been determined, but 15 gm. is usually administered three times daily with meals to patients on a daily intake of 2 to 4 gm. of sodium chloride.

Emphasis on the control of fluids and electrolytes has led to a study of their relation to the control of so-called intractable heart failure.[167] Despite the most conscientious sodium restriction and the use of mercurial diuretics, the control of edema may become impossible, and diuresis does not follow the exhibition of mercurial compounds. This has been regarded as related to an excessive reduction in glomerular filtration,[111, 168] but marked aberration in the blood electrolyte pattern has also been held accountable for the therapeutic unresponsiveness of some patients with heart failure. Frequently repeated mercurial diuresis may, as mentioned earlier, cause an excessive loss of chloride ion, relative to sodium, and may result in a hypochloremic, hypokalemic alkalosis.[76, 77] In the presence of such electrolyte and acid-base disturbance, the kidney is unable to excrete sodium and water, even under the stimulation of mercurial drugs.[78, 79, 168] This may often be prevented by the intermittent administration of ammonium chloride during the use of the mercurials, or ammonium chloride may be given to correct the alkalosis after it has developed. After such correction of the disturbed electrolyte pattern, one may again observe a satisfactory diuresis with the mercurial compounds. Complete correction of the electrolyte pattern occasionally requires the administration of potassium as well as chloride ion. Occasionally, also, ammonium chloride must be given intravenously to be effective, either because of poor absorption of the enteric-coated tablets or because of gastrointestinal intolerance.

The occurrence of the sodium-depletion syndrome and its effect on the electrolyte pattern have also been mentioned. Careful and complete electrolyte studies should be made before unresponsive cardiac failure is attributed to a sodium-depletion syndrome. The intravenous administration of hypertonic sodium chloride appears theoretically indicated and may on occasion be followed by clinical improvement.[39, 92, 168] However, the effectiveness of this measure is uncertain, and because of the undesirability (even the danger) of intravenous administration of sodium to patients in heart failure the greatest discretion must be used in this practice. Although serious blood-electrolyte disturbances undoubtedly further endanger the prognosis in cases of congestive heart failure, they are much less commonly responsible for unresponsiveness to treatment and an unfavorable clinical course than is the basic cardiac disease, associated and complicating factors or improper or incomplete execution of known therapeutic measures. Only after the adequacy of treatment has been meticulously reviewed and checked, and after remediable contributory or underlying causative factors such as hyperthyroidism, infection, anemia and so forth have been investigated and corrected, if possible, should one attribute therapeutic failure to blood-electrolyte disturbances. Even then it may be difficult or impossible to correct the electrolyte abnormalities due to complicating or irreversible cardiac or extracardiac factors — or their correction may not be adequate to stem a relentlessly fatal course due to irreversible cardiac dysfunction and its consequences.

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Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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TRACY BURR MALLORY

DR. BENJAMIN CASTLEMAN: Before beginning today's conference, I think it is fitting to pay tribute to the memory of Dr. Tracy Mallory, who, as you know, died last Sunday, November 11. I have asked Dr. Means to say a few words.

DR. J. H. MEANS: We have lost a beloved friend and a distinguished professional brother. It is fitting this morning, in this place, the scene of his labors, and at this exercise, which owes so much of its character to him, that we should pause for a moment from our busy routine and think of him.

The professional accomplishments of Tracy Burr Mallory will presently be duly recorded, no doubt, in resolutions passed in various official places. They are too numerous to be enumerated even briefly on this occasion.

Let us rather think today of our friend himself as we knew him, what he meant to us. I can remember him as a medical student, on the medical wards of this hospital. That was in 1921. My chief recollection of him as of that time is of his sincerity of purpose and his intellectual honesty, his genuine scientific curiosity. He had begun to show the very healthy skepticism that I believe was one of his striking characteristics.

I recall his coming to see me with his wife at Woods Hole in the summer of 1925. This was when we were trying to persuade him to be the successor of his father's collaborator, Dr. James Homer Wright. He thought the proposition through with characteristic thoroughness, but finally having accepted, he gave everything he had to the job with the utmost loyalty until his death. Faced with facilities that ever became more inadequate, and with a steadily increasing volume of departmental work, he maintained always his whimsical good humor and patience. His office door always stood open, and a smiling welcome there was for anyone dropping in, and wise counsel on whatever problem was presented. I used frequently to intrude on him, as did many others. Never did he say he was too busy, but always had time to listen and to discuss. Innumerable hospital and university burdens he bore unhurriedly and with equanimity. He went to war and did a magnificent job. He returned home and picked up his permanent job again without any fuss, and carried on again in his unhurried but effective manner. He saw nearly every department but his own get improved quarters and equipment, but never did he show annoyance or bitterness on that account.

These clinicopathological conferences now take the form he set. The Cabots, Richard and Hugh, who started them, discussed all the cases themselves. Tracy Mallory broadened the base, giving opportunity for most of the clinical staff to participate in rotation, and, I believe, greatly enhanced their scientific value thereby.

For all these and many other things we are grateful to Tracy.

Let us stand now for a minute in silence in memory of him.

* * *

And now, as he would have wished, carry on with the job.

CASE 37481

PRESENTATION OF CASE

A fifty-five-year-old woman was brought to the hospital because of the sudden development of inability to speak and paralysis of the right arm and leg.

The history was necessarily limited because of the patient's inability to express herself. It was learned from a companion that the patient had enjoyed good health, had been regularly employed and was having her summer vacation. On the day prior to admission she had complained of headache and "chilly feelings" during the morning; by afternoon the headache had subsided. She ate dinner that evening and later played a game of cards. The following morning she seemed well until 10:00 a.m., when she was found lying on her bed, partially dressed, unable to speak or to move her right arm and leg. She was conscious and appeared to hear and understand what was said. A physician who was called reached her bedside in time to witness a generalized convulsion. A grain of sodium phenobarbital was administered and arrangements for entry to the hospital were made immediately.

Two to three months previously she had begun "to stutter occasionally." There had been no speech impediment before that time, and the exact nature of this difficulty could not be ascertained. Previous headaches and other neurologic symptoms were not known to have occurred, nor was there a record of hypertension or vascular disease in any form. For years she had been intolerant of cold weather

*Deceased.

and had gained weight easily. The uterus had been removed because of a "benign tumor" many years previously.

Physical examination revealed a moderately obese, right-handed woman who spoke incoherently. There was a slight degree of cyanosis of the lips. Respirations were Cheyne–Stokes in type at first but soon became regular. The heart and lungs were normal except for a Grade I to II systolic murmur heard in the pulmonic area. In addition to an obvious aphasia there was a marked right hemiparesis; the lower part of the face was weak, no voluntary movement was observed in the right arm and movements of the right leg were feeble. All the tendon reflexes were present, those on the right side being slightly more active than the left; the right plantar reflex was extensor, whereas the left was flexor. The optic fundi were not remarkable. Movement in all four quadrants of the visual fields attracted her attention. The pupils were equal and reacted normally; the eyes were well centered, but ocular movements could not be tested fully. There was slight stiffness of the neck on forward bending. She was incontinent of feces.

The temperature was 99°F. and the pulse 80. The blood pressure was 170 systolic, 85 diastolic.

The white-cell count was 16,200 with 65 per cent neutrophils. The hemoglobin was 14.2 gm. The urine had a specific gravity of 1.012 and gave a + albumin reaction. The cerebrospinal fluid had a pressure equivalent to 210 mm. of water, was faintly xanthochromic and contained 76 mg. of protein per 100 cc. There were a few crenated red cells in the fluid; the Wassermann reaction was negative. X-ray films of the skull revealed a slight degree of hyperostosis of the inner table of the frontal bones. The pineal body was faintly calcified and could be seen only in lateral views, in its normal location. X-ray films of the chest showed slight hypertrophic changes in the thoracic spine, small cervical ribs bilaterally and several calcified scars in the hilar areas.

During the first four hours in the hospital there was rapid recovery of voluntary movement in the right arm and leg and more adequate movement of the face. Some words were spoken clearly, but most were not. On the second hospital day a more careful analysis of her language performance disclosed a marked tendency toward perseveration, an inability to provide the correct name for some common objects and a failure to understand completely spoken commands. She could name the days of the week and the months of the year and could count. The visual fields were full on confrontation tests. She could now move the fingers of her right hand independently, although slight right hemiparesis remained. There was no loss of sensory function, including position sense, two-point discrimination and simultaneous stimulation on both sides of the body. On the third hospital day the speech was improved, although attempts to speak rapidly caused her performance to deteriorate. She still spoke slowly and deliberately. By the seventh day only minimal weakness of the right arm and leg remained and speech was almost normal. The right plantar reflex was still extensor and the tendon reflexes were more active on the right side.

With the rapid improvement the patient was encouraged to get up and walk about her room. On the seventh day, while preparing to go out for a walk, she was observed by a nurse to lean heavily against a dressing table and to slide to the floor. She did not injure herself. Thereafter she seemed fairly well and made no complaints. At 6:00 a.m. on the following morning she vomited and was exceedingly difficult to arouse. The blood pressure was 190 systolic, 60 diastolic, and respirations were again of the Cheyne–Stokes type. She moved the left arm and leg occasionally but not the right limbs. The optic fundi were unchanged. The pupils were equal; they reacted normally but fluctuated in size from 2 to 5 mm. There were slight side-to-side movements of the eyeballs. The right arm and leg were flaccid and the reflexes as before. The neck was moderately stiff. The cerebrospinal-fluid pressure was now equivalent to 500 mm. of water and the fluid was grossly bloody. It contained 23,100 red cells, 5050 neutrophils and 500 lymphocytes per cu. mm. On other lumbar punctures made on the ninth and tenth days the pressures were equivalent to 450 and 270 mm. of water and fewer red cells.

The state of consciousness did not improve. She remained semicomatose, moaning or moving slightly only on painful stimulation. Occasional movements of the right arm and leg were noted. Coma was deeper and the plantar reflexes were extensor bilaterally on the tenth day. The blood pressure at this time was 200 systolic, 90 diastolic. The pulse was 160 and the respirations slowed to 10 per minute and became more irregular. The patient died ten days after the onset of the neurologic symptoms.

Differential Diagnosis

Dr. Charles S. Kubik*: Because of the sudden onset of the hemiplegia and aphasia, this almost from the very beginning had the appearance of a vascular lesion and, because of the headaches, of hemorrhage in particular. Later on, the diagnosis of hemorrhage was confirmed by the lumbar puncture. Knowing that, one only has to consider the nontraumatic causes of bleeding into the spinal fluid, commonly spoken of as spontaneous subarachnoid hemorrhage, although the bleeding in these cases takes place into the subarachnoid space or ventricle. By far the most common cause of such bleeding into the spinal fluid is an aneurysm of one of the main cerebral arteries — internal carotid, anterior cerebral, middle cerebral and occasionally the basilar or vertebral arteries. These aneurysms are small and, with rare exceptions, do not cause

*Consulting neuropathologist (formerly, neuropathologist and chief, Department of Neurology), Massachusetts General Hospital.

symptoms before they begin to bleed. In most cases the clinical picture is very characteristic. Outstanding features, which occur almost without exception, are extremely severe headache, rigidity of the neck and bloody spinal fluid under increased pressure. Loss of consciousness may or may not occur. In the majority of cases there are no focal signs, particularly at the onset. Because the clinical picture is so characteristic the diagnosis is usually made even before the spinal fluid is examined. The spinal fluid is usually bloody from the beginning or shortly thereafter, but once in a great while the initial bleeding may be into the substance of the brain itself without any subarachnoid hemorrhage. We have had two or three such cases, in one of which a large cerebral hemorrhage was evacuated at operation. One can understand why a hemorrhage into the brain might occur from an aneurysm of the middle cerebral artery in the sylvian fissure, where it is closed in more or less completely by brain tissue and where it may actually form a small depression in the surface of the brain. In such a case rupture might take place directly into the brain.

But there are some features that do not fit in too well with the diagnosis. The white-cell count in the spinal fluid was much higher than it is in most cases. There is usually slight to moderate elevation of the white cells, not often more than a few hundred per cubic millimeter. I have never seen a count of 5000. A more important point is that in the fatal cases there is more blood in the spinal fluid than was present in this case, and one would have expected the fluid to become more bloody subsequently, not less bloody, as in this case. The improvement that took place after the patient was admitted would fit in with that condition, and the focal signs indicating a lesion involving the motor cortex, corticospinal tracts and speech areas would be consistent with hemorrhage into the substance of the brain from an aneurysm of the middle cerebral artery.

The possibility of an intracerebral hemorrhage of the type that occurs in hypertension also has to be considered. The most common site of such a lesion is the region of the lenticular nucleus and internal capsule, but it may occur in almost any part of the brain. The course is almost invariably steadily downhill. I do not recall any case with such marked improvement as that which took place initially in the case under discussion. Then, one may ask whether this patient had hypertension. I think it is doubtful — first, because the diastolic pressure was not high, and, secondly, because there was no mention of cardiac enlargement, either clinically or by x-ray examination. It is quite possible that the moderate elevation of the blood pressure that was observed may have occurred as the result of increased intracranial pressure. I believe that cerebral hemorrhage can be ruled out.

Because of the high white-cell count in the cerebrospinal fluid, I mention the possibility of subacute bacterial endocarditis with bleeding from a mycotic aneurysm. In subacute bacterial endocarditis there may also be a mild meningitis, although the cell count is usually lower than that recorded here. However, there was nothing in the clinical manifestations that was at all suggestive of an endocarditis, and I believe that can be ruled out.

Another condition that may give rise to subarachnoid hemorrhage is a vascular anomaly, usually an arteriovenous angioma. There were some features about this case that favor that diagnosis. The abnormal blood vessels of these lesions are both superficial and deep, so that bleeding into the substance of the brain, without subarachnoid hemorrhage, is more likely to take place than with the small saccular or "congenital" aneurysm. Such a lesion might also explain the stuttering that this patient had for two or three months before the onset of the hemiplegia. It was impossible to get much information about that, but it was definitely stated that the disorder of speech was something the patient did not always have. Since it was a new development, it has to be taken into consideration, and in the light of subsequent developments it may very well have been an aphasic disorder. With these lesions convulsive seizures are common, but that does not help in the differential diagnosis because bleeding from any source in the locality that was apparently involved might have resulted in convulsive seizures. The comparatively small amount of blood in the spinal fluid, in a fatal case, might also favor such a diagnosis, and so would the xanthochromia of the spinal fluid, which was observed at the first lumbar puncture. It is unlikely that xanthochromia would take place in one day, but it might be explained by arteriovenous angioma that had been present for a long time.

To begin with, I favored the diagnosis of aneurysm with bleeding into the substance of the brain, but after further consideration of arguments, pro and con, I am inclined to think that an arteriovenous angioma is a more likely possibility.

Dr. Maurice Fremont-Smith: How high a white-cell count will be found in the fluid just from blood alone?

Dr. Raymond D. Adams: When blood is spilled into the spinal fluid one usually finds about one white cell for every few thousand red cells according to the red-cell–white-cell ratio in the blood. Since the blood is an irritant, within 24 to 48 hours there will be disproportionately high numbers of white cells — it may be as high as a few hundred, a mixture of polymorphonuclear leukocytes and lymphocytes. Of course, in counting fluids like this there is a great likelihood of error — as when the spinal fluid is not shaken well or when the decimal point is put in the wrong place.

Dr. James B. Ayer: That is true. It also depends on the speed with which it is done — whether or not there is clot in the spinal fluid. The only comment I have to make is that this case is so charac-

teristic of a middle-cerebral-artery aneurysm that I wonder why you gave it to Dr. Kubik to discuss.

Clinical Diagnosis

Ruptured congenital aneurysm with subarachnoid hemorrhage.

Dr. Kubik's Diagnosis

Arteriovenous angioma.

Anatomical Diagnosis

Glioblastoma multiforme with hemorrhage into lateral ventricle.

Pathological Discussion

Dr. Benjamin Castleman: The important findings at autopsy were all in the brain, and I shall ask Dr. Adams to present them.

Dr. Adams: The dominant features of this pathologic process were as follows: The surfaces of the brain were very flat and the subarachnoid space over the cerebral hemisphere was obliterated. The left cerebral hemisphere was somewhat wider in its midportion than the right one and there was a bulge on its medial surface. No subarachnoid hemorrhage over the surface of the brain could be seen, and at the time of autopsy some skepticism was voiced as to whether there had been a subarachnoid hemorrhage at any time. A definite left-cerebellar pressure cone was observed — and also a grooving of both hippocampal gyri by the tentorium, left more than right. The cerebral vessels were entirely free of atherosclerosis and no aneurysms were seen arising from them. On horizontal section there was a grayish-red, soft, friable mass in the body of the corpus callosum that extended almost to the genu anteriorly and well back toward the splenium posteriorly. It was of the magnitude of 2 to 3 cm. in this dimension. Lateral to this mass and extending into the central white matter of the posterior part of the left frontal lobe was a clot of dark-red blood about 3 by 4 cm. in horizontal diameter. The hemorrhage had extended into the roof of the left lateral ventricle, and a considerable amount of blood must have entered the ventricle because the prosector was able to aspirate more than 30 cc. at the time the brain was removed. The mass separated the lateral ventricles and must have deformed them to some degree.

This mass, on microscopical examination, proved to be a moderately cellular glioblastoma multiforme. Some of the cells could be identified as fibrous astrocytes; many others could not be identified but were probably undifferentiated glial cells. There were mononuclear and multinuclear giant cells, but mitoses were rare. The tumor was quite vascular in places; in some of the vessels there were thrombi of fibrin, and around some of them fresh red corpuscles had extravasated. Vascular proliferation, — that is to say, proliferation of adventitia and endothelial cells of blood vessels, — was seen in two parts of the tumor. There was also necrosis and pseudopalisading of tumor cells. All these microscopic changes will be recognized as the characteristic features of glioblastoma.

The hemiplegia and aphasia were very likely related to the extension of the tumor and to the hemorrhage into the left cerebral hemisphere. It was pretty clear that the hemorrhage had arisen in a vascular part of the tumor and probably extended beyond the border of the tumor. The terminal coma was probably due to the ventricular hemorrhage, and death was probably due to ventricular hemorrhage and cerebellar pressure cone. It is hard to explain the stuttering, for we know so little about it. Certainly the tumor of the corpus callosum extending somewhat into the white matter in the frontal lobe may have produced seizures or may have disturbed brain function in some way as early as two or three months before death. The symptoms that brought the patient into the hospital, — the hemiplegia and the aphasic disorder, — may have been caused by a focal convulsion rather than hemorrhage; all the hemorrhage that we observed appeared to be very recent, perhaps only a few hours old, and there was no older hemorrhage in the tumor or around it. The rapid recovery from hemiplegia after a convulsion may be an example of a rapidly receding postepileptic hemiplegia.

Dr. Kubik often teaches, and I entirely agree with him, that apoplexy is seldom the initial symptom of a brain tumor. It is not uncommon to see hemorrhage in glioblastoma where no apoplexy seems to have occurred during life, and a rapid accession of neurologic symptoms may occur in a case of glioblastoma where no hemorrhage is found at autopsy. Yet there are exceptional cases in which it appears that the first important neurologic event is related to hemorrhage into the tumor. I have seen apoplexy two or three times with glioblastoma multiforme and twice with medulloblastoma of the cerebellum — and, of course, with the vascular anomalies that Dr. Kubik chose as his diagnosis it is very common. Globus* has written on the subject of paralysis as a manifestation of brain tumor.

Dr. Kubik: I had originally thought of mentioning tumor as a rare cause of subarachnoid hemorrhage but decided to omit it entirely, since there had been no previous symptoms of tumor.

*Globus, J. H., and Sapirstein, M. Massive hemorrhage into brain tumor: its significance and probable relationship to rapidly fatal termination and antecedent trauma. *J. A. M. A.* **120**:348-352, 1942.

CASE 37482

Presentation of Case

A forty-one-year-old woman was admitted to the hospital because of weight loss and intermittent fatigue.

Six months prior to admission the patient developed malaise and an unproductive cough. These were variable from day to day, and she was thought

to have "flu." In spite of a fairly good appetite there was a slow but steady weight loss. Three and a half months before admission she coughed up a little bright-red blood for the first and only time and the temperature was 102°F. An x-ray film of the chest showed the lungs to be cloudy, and her physician noted heart murmurs. Two months prior to admission she was in bed for one week because of a temperature of 102°F. After this she felt less fatigued for a short time, but the feeling soon returned. One and a half months before admission there was a single episode of mild epistaxis. The physical signs were apparently unchanged at a check-up one month before admission, but four days before she entered the hospital her physician noted anemia, a change in the heart murmurs and a few red spots on the conjunctivas. On several occasions during this illness she had had pain and swelling of the ankles without redness or heat.

There was a total weight loss of 40 pounds from a pre-illness weight of 140 pounds. There was no history of rheumatic fever; she had passed an insurance examination 14 years previously.

On physical examination there were a few small red spots on the conjunctivas. There were signs of fluid in the left chest to the level of the tenth thoracic vertebra and there were moist rales at both bases. The heart was slightly enlarged to the left and there was a Grade IV, rough systolic murmur and thrill maximal at the apex and transmitted to the lung bases and a Grade I apical diastolic rumble and protodiastolic gallop along the left sternal border. The pulmonary second sound was greater than the aortic. A nontender liver was palpable 3 cm. below the costal margin. The spleen could not be felt. There was no calf tenderness or peripheral edema. Two foci of tiny linear hemorrhages were noted in the right fundus.

The temperature was 101.2°F., the pulse 120 and the respirations 24. The blood pressure was 85 systolic, 55 diastolic.

The urine had a specific gravity of 1.015, a pH of 6 and + albumin; smears and cultures were negative. Examination of the blood showed a white-cell count of 13,250, with 84 per cent neutrophils, a hemoglobin of 8.2 gm. and a hematocrit of 31 per cent. The sedimentation rate was 1.1 mm. per minute. Blood cultures obtained on the day of admission and on the fifth day grew anaerobic streptococci. Numerous other blood cultures were negative, although a number of these showed gram-positive cocci on smear. The antistreptolysin titer was 317. A tuberculin test was positive in dilution of 1:100. An electrocardiogram showed a sinus tachycardia of 120 with no other abnormal findings. A roentgenogram of the chest demonstrated prominent vascular markings and a small amount of fluid in the left pleural cavity. The heart was normal in size transversely, but there was questionable enlargement of the left auricle. An x-ray film of the teeth showed several abscesses.

The isolated streptococci were found to be inhibited by 0.5 units of penicillin; on the ninth hospital day therapy with 2,000,000 units per day was begun and an adequate blood penicillin level was maintained. On this therapy the temperature dropped from 102 to 99.8 to 100°F. and the patient improved subjectively. The pulse rate remained at about 120. Thirty cc. of fluid removed from the left pleural cavity on the eighth day contained 100 white cells per cubic mm., of which 80 per cent were neutrophils. Smear of this showed gram-positive diplococci and a culture grew *B. subtilis*. On the eighteenth and nineteenth days the patient received 500 cc. of blood with a rise in the hemoglobin level from 9 to 13 gm. On the nineteenth day she developed orthopnea, and examination revealed bilateral basal rales, moderately engorged, nonpulsating neck veins and, in addition to the murmurs previously heard, a Grade II, rough diastolic murmur heard best in the fifth intercostal space next to the sternal border and not heard higher up. The temperature was 100°F. and the pulse 120. Digitalization resulted in considerable subjective relief with only slight improvement in the objective findings. On the twenty-seventh day the patient complained of a "tightness" across the upper chest that she stated had been present for about one week. An electrocardiogram showed the Q, R, S and T waves to be lower in all leads than in the previous tracing. In the days that followed she had episodes of nausea, vomiting and dyspnea. The temperature remained at 100°F. and the pulse in the neighborhood of 120. The physical findings remained essentially unchanged. She died quietly on the thirty-fifth day.

Differential Diagnosis

Dr. Thomas Paine*: We have, then, a woman who died in the prime of her life from a wasting disease that ran its course in about seven months.

Initially there was malaise and cough, then weight loss, fever and a slight hemoptysis. These are, of course, the symptoms and signs of tuberculosis — at least until another cause can be demonstrated. At this time she was found to have "cloudy" lungs and heart murmurs. Later in the illness there developed anemia, a change in the heart murmurs, red spots on the conjunctivas and a considerable weight loss. The physical findings of importance were evidence of a wasting disease, fever, a heart enlarged to the left with signs suggesting mitral regurgitation and stenosis, signs of cardiac decompensation with left pleural effusion, rales at both lung bases, a slightly enlarged liver and what were apparently petechiae on the conjunctivas and in the right fundus.

May I see the x-ray films?

Dr. Joseph Hanelin: The films of the chest extend over a four-week period, and some change

*Assistant physician, Massachusetts General Hospital.

is noted over this course of time. The heart is certainly not enlarged in transverse diameter; left-auricular enlargement is possible and is suggested by this bulge posteriorly. Of interest are the rather prominent lung roots bilaterally with a sort of nodular outline suggesting lymphadenopathy. The lung parenchyma shows prominent linear markings and a generalized granular texture. Fluid is present at the base in only a small amount at the first examination and is slightly increased four days later. Noted in the later films and somewhat suggested by the first films is an area of partial collapse of the basal segment of the left lower lobe. There appears to be some atelectatic and pneumonitic change at the right base as well. Between the first films and those taken about two weeks later there is partial clearing of the process in the lung, but at no time have the changes totally disappeared. At all times there is persistence of what appears to be hilar adenopathy. Films of the abdomen made after the barium swallow show the stomach to be displaced toward the left by what is apparently a large liver. The films of the teeth show multiple periapical abscesses.

DR. PAINE: The history and physical findings, in conjunction with two positive blood cultures for anaerobic streptococci, mean subacute bacterial endocarditis. Two questions now arise: On what heart condition was the subacute bacterial endocarditis superimposed, and what led to the patient's death? Subacute bacterial endocarditis superimposes itself on hearts suffering from the unphysiologic hazards of congenital defects or on valves injured by rheumatic disease, syphilis or calcareous deposits. There was no evidence of syphilitic disease or arteriosclerosis, and I do not know how to rule out a congenital defect in this patient, so that leaves rheumatic heart disease, which seems most sensible, anyway.

There was no evidence of pre-existing rheumatic heart disease, although the passing of an insurance examination fourteen years previously certainly does not rule it out. On admission she had the murmurs and signs of mitral valvular disease, and someone wondered about the possibility of active rheumatic fever because an antistreptolysin titer was obtained. The result of this single test was not helpful; a rise in antistreptolysin titer might have been useful in implicating a recent, possibly activating, hemolytic streptococcal infection.

There is no way to implicate active rheumatic myocarditis on the basis of the laboratory findings given here, since these are also the findings in subacute bacterial endocarditis. The initial electrocardiogram was reported to show only sinus tachycardia; there was no mention of prolongation of the PR interval. She did have pain and swelling of the ankles on several occasions during the illness, which could indicate some activation of a rheumatic process but could also indicate right-sided heart failure.

Now, what happened to her during the subsequent course of her illness? The sensitivity of the infecting organism to penicillin was determined and she was given an amount of penicillin that should have been adequate to eradicate the infection, provided it could find its way to the organisms. But the fact is that the treatment was not a success from the patient's point of view. It would have been important to know whether or not this organism was an enterococcus. The majority of cases of subacute bacterial endocarditis are due to the so-called *Streptococcus viridans*. This organism is relatively penicillin sensitive and usually responds to penicillin therapy alone. The enterococcus, however, is relatively penicillin resistant, and the best type of therapy for subacute bacterial endocarditis caused by it seems to be a combination of penicillin and streptomycin. Unfortunately, we do not know whether this organism was or was not an enterococcus. The penicillin sensitivity in this case does not help in the differentiation, as it could be either a more sensitive enterococcus or a more resistant *Streptococcus viridans*. The patient did show a drop in fever at the beginning of penicillin treatment alone, which suggests that the drug was having an antibacterial effect.

On the day before penicillin therapy was begun, pleural fluid was obtained that showed polymorphonuclear leukocytes and gram-positive diplococci. This may indicate that organisms were also growing on the right side of the heart and that organisms reached the pleura by means of a septic embolus to the lungs, although this is unusual in subacute bacterial endocarditis.

After transfusions were given she developed increasing signs of right-sided heart failure and a new heart murmur. This murmur, — I suppose that it was on the left side of the sternum, although this is not stated, — could be that of aortic regurgitation or tricuspid stenosis. Perhaps the fifth interspace is too far down for an aortic murmur, so this may represent tricuspid-valve difficulty, and perhaps there were organisms growing there, in view of the pleural-fluid findings already mentioned.

The patient continued to run a slight fever and to have a considerable tachycardia. Then there was tightness across the upper chest along with changes in the electrocardiogram. There were several episodes of nausea and vomiting, probably the result of cardiac failure in relation to the gastrointestinal tract. Then she died quietly, after about seven months of illness and after about twenty-six days of penicillin treatment. The presence of low-grade fever throughout the period of treatment is something seen in many patients with subacute bacterial endocarditis who have been successfully treated with penicillin, so it does not necessarily represent a sign of continued bacterial activity.

Before the days of penicillin, death from subacute bacterial endocarditis was often the result of embolism from the infected valves. But now deaths

from embolism have become uncommon, possibly because local growth and extension of the bacterial vegetation is halted by penicillin, allowing more healing and better fixation of the vegetation so that parts of it are not so easily dislodged. Immediate deaths, during penicillin treatment of subacute bacterial endocarditis, have also commonly been due to congestive failure, but then the congestive failure seems related to valvular defects rather than to the myocarditis seen in the acute stage. Of course, both factors, myocarditis and valvular defect, may be so "ganged up" on the heart that it would be impossible to assign a more important role to one than to the other. One point is certain, however: the longer the treatment is delayed the poorer is the prognosis in subacute bacterial endocarditis.

Possibly the subacute bacterial endocarditis was controlled in this patient and she died of an overwhelming rheumatic myocarditis, although there is no clinical proof of this. Rheumatic fever could cause such changes as were observed in the lungs — and possibly pericarditis to account for the feeling of tightness across the chest. This symptom could also have been a result of small septic emboli to the coronary arteries, with myocardial infarction.

My diagnoses, therefore, are healing subacute bacterial endocarditis, superimposed on rheumatic damaged mitral and tricuspid valves; myocarditis, either of the sort related to subacute bacterial endocarditis or of a rheumatic nature, or both; cardiac decompensation, with pulmonary and hepatic congestion; and pulmonary infarcts, secondary to the subacute bacterial endocarditis of the tricuspid valve.

Dr. Edward F. Bland: Dr. Paine, would you comment on whether or not the treatment should have been more vigorous? After all, 2,000,000 units of penicillin is now considered fairly minimal. The temperature chart is of some interest; this patient was never afebrile at any time, had a tachycardia of 120 and obviously was not getting well.

Dr. William S. Clark: She was also receiving benamid.

Dr. Paine: This chart does demonstrate considerable fall in fever at the time of administration of penicillin treatment, although it remained around 100°F. except for an occasional spike above that. If the organism was really sensitive to 0.5 units of penicillin in vitro, then the chances are that 2,000,000 units a day would be sufficient to take care of the infection. Certainly many patients with subacute bacterial endocarditis do have a low-grade fever (temperature up to 100°F.) during the penicillin treatment that disappears when the penicillin is stopped. I think the tachycardia was related to underlying myocarditis, which these patients certainly may have, either on the basis of small infarcts to the myocardium or other factors that we do not know about or on the basis of rheumatic activity going on at the same time.

Dr. Bland: A less important detail is the early blowing diastolic murmur along the left sternal border.

Dr. Paine: It could fit in with aortic involvement.

Dr. Paul D. White: I thought you inferred that the diastolic murmur may have been tricuspid.

Dr. Paine: I thought it may have been — particularly since there were organisms in the pleural fluid suggesting bacterial growth on the right side of the heart.

Dr. White: Do you think there were two organisms?

Dr. Paine: No; I do not know of any logic to bring in tuberculosis when there were several positive blood cultures for the streptococcus. An enterococcus, which may produce small abscesses in the myocardium, may have been responsible for the lung findings and possibly for the lymphadenopathy.

Dr. White: You do not think there could have been both?

Dr. Paine: I doubt it.

Dr. Bland: You considered it to have been an enterococcus?

Dr. Paine: I think it could have been that. It was described as an anaerobic streptococcus.

Dr. White: A coronary embolism might explain some of the distress across the chest, but the electrocardiographic changes were not striking enough to support that possibility.

Dr. F. Dennette Adams: Would a ruptured valve explain this change in the murmur — and also the pain?

Dr. White: Usually a ruptured valve gives a much louder murmur.

Dr. Bland: We saw this patient in Cardiac Grand Rounds. We were very much interested in the physical signs because one of the murmurs, the loud systolic murmur, was quite close to the sternum.

Dr. Allan Friedlich: The apex was palpable very close to the sternum, so it was difficult to interpret the significance of the rather loud harsh systolic murmur located at the apex. We speculated on whether it could have been due to a ventricular septal defect with growth on the right-ventricular endocardium or possibly a rather extensive mitral lesion. The intensity of the murmur suggested the possibility of a ruptured chorda.

Clinical Diagnoses

?Rheumatic heart disease with mitral insufficiency.
Subacute bacterial endocarditis.
Subacute myocarditis.
?Diffuse glomerulonephritis.
??Disseminated lupus erythematosus.

Dr. Paine's Diagnoses

Subacute bacterial endocarditis, healing.
Myocarditis, ?rheumatic, ?due to subacute bacterial endocarditis.

Cardiac decompensation with pulmonary and hepatic congestion.
Pulmonary infarcts.

Anatomical Diagnoses

Endocarditis, subacute, bacterial (anaerobic streptococcus), with involvement of mitral valve and left auricle.
Coronary embolus, septic, left anterior descending.
Myocardial abscess, left ventricle.
Rupture of chordae tendineae, anterior cusp of mitral valve.
Cerebral aneurysm, mycotic, multiple, unruptured.
Infarct of heart, kidney, spleen and cerebellum.
Pulmonary edema.
Hydrothorax and ascites.

Pathological Discussion

Dr. Benjamin Castleman: The heart was not enlarged and the mitral valve showed thin and long chordae tendineae without any evidence of any thickening to suggest previous disease of a rheumatic nature. On the anterior cusp there were granular yellowish vegetations that extended downward along a chorda tendineae that had ruptured. There were also a few vegetations on the posterior cusp and on the auricular endocardium, but microscopical sections showed no evidence of any underlying rheumatic infection, either in the left-auricle wall or in other sections of the myocardium. Thus we have here evidence of a bacterial endocarditis with rupture of the anterior cusp of the mitral valve but without any underlying disease. The wall of the left ventricle was soft and mottled and on section seemed to be infarcted. In this photograph of the surface of the heart you can see the cut end of the descending branch of the left coronary, which is perfectly patent (just to the left of the vertical arrow), and here just under the vertical arrow you see an embolus protruding from the vessel (Fig. 1). Surrounding this vessel with the embolus is an abscess (horizontal arrow) produced by rupture of a mycotic aneurysm of this vessel. A section of the wall was partially replaced by necrotic tissue with a polymorphonuclear infiltration.

Dr. White: How old a process is this?

Dr. Castleman: I do not know how long this embolus has been there, but I suppose it occurred eight days before death, when the patient complained of chest tightness. A section of the valve through the endocardium was packed with streptococci and a culture of the abscess showed anaerobic streptococci. There were emboli to the kidney and spleen, producing infarcts in those organs. There were also about 4 or 5 mycotic aneurysms in the brain, one or two of which had apparently leaked, because there was some old blood around them but none had ruptured. We are quite sure that the disease had been going on for probably six months, and there is certainly good evidence at autopsy that the patient was not at all responsive to the antibiotics. We found myriads of organisms in the vegetations. There was no disease of any other valve and no congenital anomaly. The lungs showed a fair amount of edema but no infarcts.

Dr. Bland: Dr. Paine, is it not true that the enterococcus must always be treated very vigorously?

Dr. Paine: Yes; that is why we should find out if an organism is an enterococcus. There is no excuse for not knowing that the organism is an enterococcus when one starts treatment for subacute bacterial endocarditis.

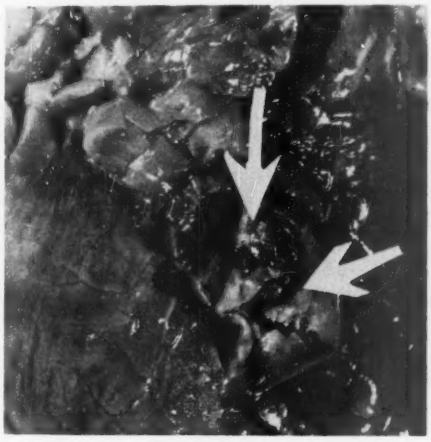

Figure 1.

A Physician: It was not a heat-resistant organism.

Dr. Paine: Unfortunately, there was another case in which an enterococcus was not reported because of a defect in the way the heat treatment was set up; hence we cannot rely on that one determination.

Dr. White: The patient's teeth were a possible source.

Dr. Bland: Is it very difficult to spot the enterococcus bacteriologically?

Dr. Paine: It is not absolutely clear cut, but most strains of enterococci are heat resistant and will grow in high concentrations of salt and at pH's that ordinary streptococci will not grow in, so actually in most cases it is not difficult to pin down.

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SENSITIVITY OF BACTERIA TO ANTIBIOTICS

Antimicrobial agents are presumed to be effective in the treatment of infections primarily, if not entirely, because of their direct action on the infecting organisms, by either destroying them or preventing their multiplication until immunity develops. The susceptibility to this lethal or inhibiting action of antimicrobial agents varies with the agents and with the micro-organism. For purposes of quantitation and comparison, the degree of this susceptibility, which is generally referred to as the "sensitivity" of the strain, is expressed in terms of the minimum concentration of the chemical or antibiotic that is required to obtain the desired result. Obviously, such tests are limited to micro-organisms that can be cultivated in the test tube. The effectiveness of antibiotics against viral and rickettsial diseases must be tested by their preventive or curative effects in experimental or spontaneous infections.

There are many factors that may influence the results of the in-vitro tests for sensitivity — that is, that may affect the value assigned to the sensitivity of an organism to any given agent at the conclusion of the test. These factors may include the type and composition of the culture medium (for example, the presence and concentration of salt, glucose and serum or blood), the pH of the medium, the number of organisms inoculated, the presence or development of factors within the medium that may specifically inactivate the antibiotic (for example, penicillinase), the length of the period of incubation and many others. Furthermore, the choice of the end-point for the test, — whether one insists on complete sterilization of the culture or on some arbitrary amount or degree of inhibition of growth, — may also markedly affect the answer that the test gives. Any of these factors, in turn, may influence the result of the same type of test differently, depending on the combination of organism and antibiotic that is being tested. Finally, in the case of some antibiotics, notably aureomycin, the rapid rate of deterioration of the antibiotic during the course of the incubation may give an entirely erroneous impression of its relative effectiveness as compared with other antibiotics that are not similarly influenced by the conditions of the test, and this impression may be entirely contrary to the results actually observed in the therapeutic effects in patients.*

The use of tests for sensitivity of bacteria as clinical guides for the selection of chemotherapeutic agents is based on the assumption that the effectiveness of these agents in therapy of an infectious disease parallels the results of the in-vitro tests with the causative organism of the infection. In other words, it is assumed that if the organism is killed by concentrations of the antibiotic that are attainable in the body the infection is one that should

*In this connection, it is of interest that some of the antibiotic disks or tablets presently being supplied commercially to laboratories for the rough estimation of sensitivity of bacteria contain smaller amounts of aureomycin than of other antibiotics, thus tending to exaggerate this impression still further.

yield to therapy with that antibiotic. Unfortunately, the concentrations of the antibiotic that are present at the site where the organism is multiplying cannot readily be measured in most cases. This, of course, will vary considerably with the dosage regimen, as well as with the route of administration and with the manner in which the particular antibiotic is absorbed, distributed and excreted in the body. Moreover, the number and concentration of organisms present at the site of infection and the constituents of the environment for the growth of the organism in vivo may have little or no relation to the corresponding features of the in-vitro tests.

How widely divergent in-vitro test results can be has been strikingly brought out in a recent paper from the Thorndike Memorial Laboratory.[1] Even with tests set up simultaneously, using the same media and the same antibiotic solutions, wide ranges of values were obtained for the minimum inhibiting concentration of any one antibiotic for any given organism, depending on the method used. Discrepancies in the results were least frequent with penicillin; even with this agent, however, although one organism showed as little as a 16-fold difference between the maximum and minimum values obtained by different tests, another organism yielded values that varied 1024-fold. The greatest discrepancies, as might be expected, were noted in the tests with aureomycin. Among seven organisms tested, the differences between the maximum and minimum values that could be assigned to the sensitivity of any one strain varied from 128-fold to 2048-fold, depending on the tests used and on their interpretation. Such divergent results must be extremely confusing to clinicians, many of whom may be willing and anxious to place complete reliance and perhaps responsibility on the laboratory for the choice of an antibiotic in the treatment of infections.

It is possible to limit these discrepancies to some extent by adopting a standard procedure. With most of the common methods, when the materials and other details of the method and the interpretation of the tests are standardized it is possible to obtain results in which there is only a 4-fold difference between the maximum and minimum values obtained when the same organism is repeatedly tested for sensitivity to the same antibiotic.[2] This 4-fold range, however, approaches the difference between the minimum effective and the maximum tolerated systemic doses of most of the antibiotics, other than penicillin, that are now available. Ideally, the procedure selected would be the one that would yield results most nearly parallel to those obtained in therapy. Unfortunately, it is not now possible to make such a selection, as might readily be deduced from the foregoing discussion. Clinicians cannot, therefore, place undue reliance on the results of tests for sensitivity and must appreciate their limitations.

In discussing their observations, the Thorndike workers[1] did not wish to imply that tests for sensitivity of bacteria to antibiotics have no value whatever. They suggest that such tests should most properly be used as a general qualitative guide to distinguish the susceptible from the nonsusceptible organisms. By standardizing the details of the method, it may be possible to obtain values that may be useful in visualizing the relative susceptibility of different organisms or of different strains of the same species to any given antibiotic. The application of a single method in this manner to a large number of strains of a variety of different pathogenic bacteria carried out at the Thorndike Laboratory has already yielded information that may prove useful for clinical purposes. Data thus obtained have indicated, for example, that strains of some species of organisms such as gonococci, Group A hemolytic streptococci and pneumococci are more or less uniform in their sensitivity to any given antibiotic. In the case of other organisms, on the other hand, individual strains may vary widely in this respect. Staphylococci, enterococci and proteus organisms are notable examples of the latter.

It therefore appears most important to place the emphasis where it really belongs — on the determination of the true causative organism of any infection. When that is done, antibiotic therapy can be selected intelligently for most infections without resort to tests for sensitivity except when one is dealing with causative organisms different strains of which have been shown to exhibit wide variations in their susceptibility to the antibiotics under con-

sideration. The adoption of such an attitude on the part of clinicians will greatly alleviate the burdens of the laboratories, which are now constantly flooded with requests for determination of bacterial sensitivity. This does not, however, relieve the clinician or the laboratory of the responsibility for obtaining proper materials for the cultural diagnosis of the etiologic agent of the patients' infections whenever that is possible and indicated.

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1. Jackson, G. G., and Fin'and, M. Comparison of methods for determining sensitivity of bacteria to antibiotics *in vitro*. *Arch. Int. Med.* **88**:446-460, 1951.
2. Erlanson, P. Determination of sensitivity *in vitro* of bacteria to chemotherapeutic agents, with special reference to routine tests. *Acta path. et microbiol. Scandinav.* Supp. **85**:1-162, 1951.

DISPOSITION OF RARE BOOK COLLECTIONS

Tufts College Medical School has recently acquired by gift the library of Dr. Joseph H. Pratt, collected over a period of years. This collection, numbering hundreds of volumes, contains many outstanding classics in the field of medicine. In like manner, although further afield, Dr. Erik Waller has given to the Uppsala University Library his remarkable collection on the history of medicine in all its fields — a collection especially rich in early printed books and containing many unique items.

Dr. Waller began to collect books in 1910, when he was a young surgeon in Sweden. Previously he was interested in manuscripts and autographs, but gradually his interest centered on the printed book. The collection now comprises about 23,000 volumes and several thousand reprints, the main portion consisting of older medical literature, including 150 incunabula. The sixteenth-century books are numerous, the collections of Ambroise Paré, William Harvey and Paracelsus being especially noteworthy for their completeness. Waller devoted much effort to collecting the old Scandinavian medical literature and his results are unrivaled by any private collector in this field.

There have long been two schools of thought on the disposition of outstanding libraries. The first is to dispose of them by sale, for the purpose of giving other collectors the pleasure of acquiring treasures for their collections. The second is to give the libraries intact to permanent institutions, where they will be preserved indefinitely for the community of scholars.

Thus the libraries of Harvey Cushing and Arnold Klebs went to Yale by gift, that of Edward Streeter to the New York Academy by purchase. Dr. William N. Bullard gave his collection of incunabula and other early medical books to the Boston Medical Library, with a considerable endowment for its maintenance. The result is an outstanding library of incunabula, now numbering approximately 800 titles.

Collections need not be of large proportions and may be devoted to a single subject. Recently Dr. Arthur B. Lyon presented to the Boston Medical Library his collection of medical fiction, gathered over a number of years. A notable example of a collection of literature on a particular subject is that on suicide, presented to the Library by Dr. A. Warren Stearns. It constitutes a valuable aid to research.

In these times of high prices, it is important that famous libraries and special collections should be placed in permanent institutions, where they will be of lasting value to scholars. Provision for this may be made early in the life of the owner by a deed of gift, the property being retained until his death, when it is automatically transferred to the institution named in the deed, without death duties or other forms of taxation. If possible, a suitable endowment should be provided to maintain and continue such a collection, which will thus become more valuable from year to year and provide an enduring monument to the donor.

THE AMERICAN ACADEMY OF CEREBRAL PALSY

The American Academy of Cerebral Palsy has recently held its fourth annual meeting in Boston, at the Copley Plaza Hotel. This relatively new organization, founded by the pioneers in the field of cerebral palsy and child development, responded to the need of co-ordinating the various medical disciplines on the problems of the brain-injured child. The recognition that the rehabilitation of the orthopedically handicapped child required contributions from many diversified specialties also

was a determining factor in the formation of the academy.

These views were reflected in the papers presented at this meeting. Results of certain cases of cortical ablation in hemiplegia were discussed by Dr. Wilder Penfield of Montreal. Dr. Franc Ingraham of Boston reported on diastematomyelia. The pathological and clinical aspects of kernicterus were reviewed by Drs. Sidney Farber and Louis Diamond of Boston, and clinical evaluation, physiology of motor learning and functional methods of orthopedic surgery were variously discussed. Dr. Arnold Gesell of New Haven presented a new film on the embryology of behavior.

This meeting culminated the twenty-odd years of experience of the retiring president, Dr. Bronson Crothers of the Boston Children's Medical Center, who was the first to recognize that the needs of the cerebral-palsy patient should be met not only in childhood but through adolescence and adulthood.

The Academy has long recognized that various nonmedical aspects of the disease are as important as the medical ones; hence many speakers from different professional fields, primarily educators and psychologists, have addressed the academy since its institution.

Attempts to correlate pathologic findings with clinical findings have been actively under way during the past two years, through a "brain registry" under the direction of Dr. Herman Josephy, who is collecting data from various parts of the country.

Another important concern of the academy has been the investigation of training resources and the establishment of standards for training personnel in this field.

The cure of cerebral palsy as such is still impossible, as many cases are caused by irreversible lesions acquired during gestation, delivery and the neonatal period. The goal should be rehabilitation of the patient — that is, the most efficient use of whatever resources are still unimpaired or can be restored by adequate therapy. The need of a team approach in evaluating and habilitating the cerebral-palsy patient is emphasized.

Habilitation depends on the holistic approach. Cerebral palsy, in addition to being a challenging medical problem, has important socioeconomic aspects that need further exploration, since today's primary aim is to integrate as many as possible of these patients into society.

The celebrated pain-killer, a secret composition sold extensively in Boston, is said to have made the proprietor, a clergyman residing in Providence, R. I., very rich.

Boston M. & S. J., *December 3, 1851*

NEW HAMPSHIRE MEDICAL SOCIETY

The following officers were elected at the annual meeting of the society, held on October 1.

President: B. Read Lewin, M.D., Claremont.
Immediate Past President: Harris E. Powers, M.D., Manchester.
President-elect: Joseph N. Friborg, M.D., Manchester.
Vice-president: Raymond H. Marcotte, M.D., Nashua.
Secretary and Treasurer: Deering G. Smith, M.D., Nashua.
Trustee (three years): George C. Wilkins, M.D., Manchester.
Speaker, House of Delegates: Louis C. Theobald, M.D., Exeter.
Vice-speaker, House of Delegates: Frederick S. Gray, M.D., Portsmouth.
Necrologist: Ralph W. Tuttle, M.D., Wolfeboro.
Delegate, American Medical Association: Deering G. Smith, M.D., Nashua.
Alternate delegate, American Medical Association: Howard P. Sawyer, M.D., Brookfield.
Councilor, Hillsborough County: Norman W. Crisp, M.D., Nashua.
Councilor, Rockingham County: Willard C. Montgomery, M.D., Epping.
Councilor, Strafford County: Samuel J. King, M.D., Rochester.
Councilor, Belknap County: Douglass W. Walker, M.D., Laconia.

The 1952 combined session of the New Hampshire and Vermont State Medical Societies will be held September 7-9 at the Mount Washington Hotel, Bretton Woods, New Hampshire.

NEW HAMPSHIRE AND VERMONT COMBINED ANNUAL MEETING

The New Hampshire and Vermont Medical Societies again held a joint session in 1951, meeting on September 30 and October 1 and 2 at the Equinox House, Manchester, Vermont. The gathering constituted the one hundred and sixtieth annual meeting for the New Hampshire Society and the one

hundred and thirty-eighth for the Vermont Society. Concomitantly the Woman's Auxiliaries to the New Hampshire and Vermont societies held their twenty-sixth and second meetings, respectively.

In addition to the usual business sessions of the houses of delegates of the two societies, combined general scientific sessions were held, and the New Hampshire Heart Association and Pediatric Societies had their annual meetings.

The speakers at the first general session on October 1 were Dr. Chester S. Keefer, of Boston, on "Present-Day Evaluation of Antibiotics," Dr. J. S. L. Brown, of Montreal, on "Basic Considerations in the Use of ACTH and Cortisone," Dr. John P. Merrill, of Boston, on "Hypertension" and Dr. John Rock, of Boston, on "Physiology of Conception: Its Disorders and Treatment." The same speakers elaborated further on their subjects during the second session, held on the following day.

A number of section meetings were held, and a group of "extra sessions" was arranged as an added feature of this year's combined meeting. These consisted of a forum on medical public relations, a round-table discussion of alcoholism, a presentation of the American Red Cross Blood Bank Program, meetings of the Vermont State Fracture Committee and the Vermont Heart Association and a Dutch-treat cocktail party.

Lay forums were conducted on medical public relations and selective service, and wide interest was shown in the 50 scientific and technical exhibits.

United States Senator Ralph E. Flanders of Vermont came from Washington to report on the national and international situations, and the Honorable Lane Dwinnell, speaker of the New Hampshire House of Representatives, discussed the part that the threat of socialistic controls had played in prompting physicians to take the necessary steps toward better medical-society organization.

The New Hampshire society passed the following resolution, emphasizing the need of an adequate supply of nurses to care for patients:

> Be it resolved that the New Hampshire Medical Society believes that the requirements for approved schools of nursing in this state should be sufficiently high to ensure well-trained nurses. These requirements must be formulated to meet the conditions in New Hampshire and be reasonable so that they can be met by the hospitals in this state. The physicians of New Hampshire are interested in having an adequate supply of good nurses to care for their patients, and believe that every effort should be made by the various interested agencies, including the Board of Nurse Examiners, to achieve this result.

A Claremont surgeon, Dr. B. Read Lewin, was elected president of the New Hampshire society, and Dr. Wilmer W. Angell of Randolph was chosen to head the Vermont society. In 1952, for the third time in as many years, the two societies will hold another combined meeting on September 7, 8 and 9 at the Mount Washington Hotel, Bretton Woods, New Hampshire.

CORRESPONDENCE

MASSACHUSETTS SOCIETY FOR RESEARCH IN PSYCHIATRY

To the Editor: I wish to draw your attention and the attention of your readers to the functions served by one of the younger professional societies of the state, the Massachusetts Society for Research in Psychiatry, as I believe it has a commendable purpose and record.

On March 28, 1940, Dr. Edgar C. Yerbury, then Director of Mental Hygiene and Research for the Department of Mental Health of this state, organized a meeting of representative psychiatrists of Massachusetts public and private mental hospitals known to be interested in research. At this meeting Dr. William Malamud was elected the first president of this new organization after acceptance of his plan of organization and statements of purpose. He and other experienced investigators had for some time seen the need for a society to serve as a forum for young research workers in this state who were interested in the problems of mental illness. This Society from the first has encouraged early reports on research work in progress and has endeavored to help research workers with suggestions and criticism. Original reports of research were made by members of the society at quarterly meetings and the majority of these reports achieved publication in recognized national professional journals.

This society has now completed ten full years of continuous, fruitful activity and has an active membership of over 100 research-minded specialists. A new group, with youthful vigor, is continually gaining help in research and valuable training in the presentation of significant findings. Abstracts of the proceedings of this society are now regularly published in the *Journal of Nervous and Mental Diseases.*

The Society invites all young workers in psychiatric research to participate; those having material on which to report should contact the society's program chairman, Dr. Milton Greenblatt, at the Boston Psychopathic Hospital.

WILLIAM L. HOLT, JR., M.D., *President*
Massachusetts Society for Research in Psychiatry
Boston, Massachusetts

BOOK REVIEWS

Diseases in Old Age: A clinical and pathological study of 7941 individuals over 61 years of age. By Robert T. Monroe, M.D. 8°, cloth, 407 pp. Cambridge: Harvard University Press, 1951. $5.00.

The Peter Bent Brigham Hospital, opened in March, 1913, has long been noted for its finely kept typewritten patients' records. As a former house officer, the reviewer can testify concerning the meticulousness of these recordings. Dr. Harvey Cushing took advantage of them in his numerous monographs and Dr. Monroe in turn has examined nearly 8000 reports on persons over the age of sixty-one who entered the medical service during a period of thirty years up to 1943. The analysis of the records forms the basis of this book. The sample is adequate. About an equal number of men and women were admitted, mostly of the underprivileged class, to this teaching hospital. The diagnoses were frequently the consensus of several staff physicians.

The study reveals primarily the incidence of the major forms of disease in persons over sixty. For details this excellent monograph must be consulted. Insurance physicians, public-health officials, those in charge of geriatric clinics, writers of textbooks and all interested in the problems of aging will find this book invaluable. Of particular importance is the final chapter on the community resources essential for old persons. Every community in the United States should be alert to the sound pronouncements of the author.

The book is finely written and the tables exceptionally clear, with bold-face type; there is an adequate index but an all too brief list of references. The 91 tables make for quick reference, but they should be listed separately in the preliminary pages. It is hoped that Dr. Monroe's ideas on the minimum-wage and accident-liability laws and on company pension plans will not go unheeded.

HENRY R. VIETS, M.D.

The Human Colon: An experimental study based on direct observation of four fistulous subjects. By William J. Grace, M.D., Stewart Wolf, M.D., and Harold G. Wolff, M.D., with a foreword by Alan Gregg, M.D. 8°, cloth, 239 pp., with 112 illustrations. New York: Paul B. Hoeber, Incorporated. $7.50.

The authors made a direct study of the mucous membrane in four human subjects with exposed colonic tissue after operations. They measured contractile activity, mucous and lysozyme secretion, color changes and the effect of various reflex changes on the size, shape and appearance of the segments. The colon was intermittently active, with disturbed function reflected by many causes. The hypodynamic response, resulting in constipation, was encountered when the patients reacted to noxious stimulation, with feelings of fear, dejection, futility or defeat, dissatisfaction, boredom, tension and mild depression. Defecation reflexes were inhibited or eliminated under these circumstances. In general, reaction of this type was considered a general reaction of "grimly holding fast" under circumstances that threatened the patient.

The hyperdynamic reaction of the colon, with diarrhea, on the other hand, was found in response to the common irritants. In addition to directly acting stimuli the emptying reaction was also evoked by symbolic assaults, words or events with special meaning for the patient that elicited anger, resentment, guilt, humiliation, anxiety or conflict. Patients with ulcerative colitis reacted with colonic hyperfunction far more commonly and for more sustained periods than did those with normal colons. Vagotomy did not alter the behavior of the colon in patients with colitis, but in general patients with this disease were, although outwardly calm, abnormally disturbed by feelings of intense hostility, resentment and guilt. Changes involving colonic hyperfunction, at first altogether functional and transitory, may, when unduly sustained, result, according to these investigators, in structural damage and disease.

The book is an excellent example of teamwork in clinical investigation. The number of cases observed, however, is far too small to justify more than vague general conclusions. Many may believe, with some justification, that the authors' interpretation of their findings correlating life situation, emotion and bodily disease are not firmly based but reflect the trend of the times in psychosomatic overelaboration. The book, moreover, hardly projects "a fresh and provocative thesis," as postulated in the enthusiastic foreword. The effects seen in this limited field have been either observed or postulated by others, particularly Cannon, Lium, Alvarez, Almy, Cobb and Benjamin V. White.

The book is well written, with only a few errors. The glazed, heavy text paper is hard on hand and eyes. The tipped-in color plates are good but are too easily detached. References are adequate. The date and place of publication are annoyingly omitted from the title page.

HENRY R. VIETS, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Cancer as I See It. By Henry W. Abelmann, M.D. 16°, cloth, 99 pp. New York: Philosophical Library, Incorporated, 1951. $5.00.

In this small book Dr. Abelmann has endeavored to show the factors suggesting the germ-virus nature of cancer.

Chronic Ulcerative Colitis (Thrombo-ulcerative colitis). By J. Arnold Bargen, M.D., Division of Medicine, Mayo Clinic, Rochester, Minnesota. 8°, cloth, 61 pp., with 2 illustrations. Springfield, Illinois: Charles C Thomas, 1951. $2.00.

This small monograph discusses the diagnosis, complications and treatment of a serious disease, with emphasis on treatment.

Introduction to Surgery. By Virginia Kneeland Frantz, M.D., associate professor of surgery, College of Physicians and Surgeons, Columbia University, and associate attending surgical pathologist, Presbyterian Hospital, New York; and Harold Dortic Harvey, M.D., assistant professor of clinical surgery, Columbia University College of Physicians and Surgeons, and associate attending surgeon, Presbyterian Hospital, New York. 12°, cloth, 232 pp. New York: Oxford University Press, 1951. $2.75.

This second edition of a popular manual has been revised to conform to various suggestions and comments.

The Physiology and Pathology of Hemostasis. By Armand J. Quick, Ph.D., M.D., professor of biochemistry, Marquette University School of Medicine. 8°, cloth, 188 pp., with 18 illustrations and 21 tables. Philadelphia: Lea and Febiger, 1951. $4.00.

In this monograph the author presents a new theory of the coagulation of the blood and a unified concept of hemostasis. He discusses the classification, diagnosis and surgical treatment of hemorrhagic diseases. There is a special chapter on venous thrombosis. The text is divided into two parts: clinical, and laboratory methods. The section on methods constitutes half of the text and is comprehensive in scope. The chapters in the clinical part are documented with bibliographies. There is an index, and the publishing is excellent. The book should be in all collections on the subject.

Master Your Mind. By Samuel Kahn, M.D., Ph.D. 12°, cloth. New York: Rockport Press, Incorporated, 1951. $3.00.

This small book, now in its second edition, is written primarily for students. It discusses the mechanics of studying, thinking and reasoning, and memorizing and remembering. There are chapters on the use of a library, reference material, making a bibliography and taking notes.

Modern Medicine Annual, 1951. (An annual volume containing the articles that appeared in the twenty-four issues of *Modern Medicine* during 1950.) 12°, cloth, 1125 pp., with illustrations and tables. Minneapolis: Modern Medicine, 1951.

In this volume the various articles appearing in *Modern Medicine* during 1950 have been sorted and arranged according to subject. Two new chapters have been added, on "surgical technigrams" and "questions and answers." The first describes sound operative technics for common conditions. The second are practical solutions to actual situations that have been presented to the Consultant Board for solution. There is a comprehensive index of subjects and an index of authors.

A Synopsis of Surgical Anatomy. By Alexander L. McGregor, M.Ch. (Edin.), F.R.C.S. (Eng.), senior surgeon, Johannesburg General Hospital, and lecturer in surgery, University of the Witwatersrand. With a foreword by Sir Harold Stiles, K.B.E., F.R.C.S. (Edin.). Seventh edition. 12°, cloth, 778 pp., with 746 illustrations. Baltimore: The Williams and Wilkins Company, 1950. $6.50.

This British manual was first published in 1932; its popularity is attested to by a total of fifteen editions and reprintings to date. This edition has been completely revised. New chapters have been added on transthoracic surgery and surgery of the blood vessels. The sections on surgery of the sympathetic nervous system have been changed considerably, and a new section has been added on the cervicobrachial syndrome. The section on the anus has been brought up to date. Seventy new illustrations have been added to the text. There is a comprehensive index. The printing was done in Great Britain.

The Microkaryocytes: The fourth corpuscles and their functions. By K. G. Khorozian, M.S., M.D. 8°, cloth, 969 pp., with 252 illustrations and 19 tables. Boston: Meador Publishing Company, 1951. $12.00.

In this large volume the author describes his discovery of the fourth corpuscular cell and its function in the body. He contends that the so-called "blood dusts" are in actuality these newly discovered cells and that metabolism and catabolism are dependent on these cells. The book is well published and profusely illustrated.

Modern Trends in Paediatrics. Edited by Sir Leonard Parsons, M.D., F.R.S., F.R.C.P. 8°, cloth, 600 pp., with 110 illustrations and tables. New York: Paul B. Hoeber, Incorporated, 1951. $12.00.

This composite work, written by 21 eminent British specialists, deals with the child in health and disease. In addition to the ordinary pediatric conditions there are chapters on the lipoidoses, steatorrhoea, cardiovascular surgery, preventive pediatric services and child-health institutions. The various chapters are concluded with lists of references. There is a good index and the publishing is excellent. The printing was done in Great Britain. The book should be in all medical libraries and in the collections of pediatricians.

Transactions of the American Goiter Association: 1950 (annual session, March 9–11, Houston, Texas). 4°, cloth, 445 pp., with illustrations and tables. Springfield, Illinois: Charles C Thomas, 1951. $11.50.

The annual meeting of the association was devoted to a number of symposiums on various aspects of goiter, including an important one on diagnostic methods in the study of human thyroid disease. The volume is well published and should be in all medical libraries and in the collection of specialists on the subject.

I Took It Lying Down. By Marian Spitzer. 12°, cloth, 247 pp., New York: Random House, 1951. $2.75.

In this book Mrs. Spitzer, a well-known writer, tells the story of her illness from tuberculosis and her final recovery. She writes in a pleasing manner and with humor. The volume should be in all collections of popular medical books.

Enzymes and Enzyme Systems: Their state in nature. Edited by John T. Edsall. 8°, cloth, 146 pp., with illustrations and tables. Cambridge, Massachusetts: Harvard University Press, 1951. $2.75.

This small book is the joint effort of eight specialists in their particular fields. It is an outgrowth of a symposium on the state in nature of proteins and protein enzymes. It is also the first volume in a new series entitled *Memoirs of the University Laboratory of Physical Chemistry Related to Medicine and Public Health of Harvard University.* The small volume provides in easily accessible form a view of the latest developments in this field. It is well published and should be in all collections on the subject.

Administrative Medicine. Edited by Haven Emerson, A.M., M.D. 8°, cloth, 1007 pp., with tables. New York: Thomas Nelson and Sons, 1951. $10.00.

The papers included in this comprehensive work were first published in *Nelson's Loose-Leaf Medicine.* A large group of specialists wrote the various papers, which are divided into four sections: the organized care of the sick; administration and economics of medical care; public-health administration; and performance of public-health services. A good index has been provided and the book is well published. The price is surprisingly low for the size of the volume. The book is recommended for all medical libraries and should be in all hospitals.

The Doctor: His career, his business, his human relations. By Stanley R. Truman, M.D. 8°, cloth, 151 pp. Baltimore: Williams and Wilkins Company, 1951. $3.00.

Dr. Truman has written a book for the medical student and physician covering the practical side of medicine from the choosing of his field to his professional and public relations. An appendix presents the principles of medical ethics of the American Medical Association. There is also a check list of things to do when a physician begins practice. There is a good index and the volume is well printed. It should be in all medical libraries and available to all medical students and physicians.

Progressive Resistance Exercise: Technic and medical application. By Thomas L. DeLorme, M.D., assistant in physical medicine, Massachusetts General Hospital, and consultant in physical medicine, Long Island Hospital, Boston; and Arthur L. Watkins, M.D., assistant clinical professor of medicine, Harvard Medical School, and chief of physical medicine, Massachusetts General Hospital. With a foreword by Joseph S. Barr, M.D. 8°, cloth, 245 pp., with 89 illustrations and 13 tables. New York: Appleton–Century–Crofts, Incorporated, 1951. $5.00.

The principles and technics of the remedial form of exercise are fully described, and there are special chapters on fractures, knees, hips, neurologic conditions and adolescents. There is a good index. The book is well illustrated and well published. It should be in all collections on orthopedics and physical medicine.

Behandlung diabetischer Kinder: Ein Leitfaden fur die Praxis. By Priv.–Doz. Dr. Karla Weisse, Oberarzt der Univ.–Kinder–Klinik, Frankfurt-am-Main. 8°, paper, 72 pp., with 9 illustrations. Stuttgart: Georg Thieme, 1951. DM 4.90.

This small manual is devoted to diagnosis and treatment. There is a special chapter on treatment with frozen food and its prognosis.

Good Food for Diabetics. By Eleanor R. Sigel. 12°, cloth, 144 pp., with tables. New York: Harper and Brothers, 1951. $2.50.

This new cookbook for the diabetic has been written for persons who use insulin as well as for those who depend on diet alone. There is a good index and the small book is well published.

NOTICES

ANNOUNCEMENT

Dr. Elmer E. Hinton announces the opening of his office for the practice of internal medicine at 264 Beacon Street, Boston.

THE BAY STATE HOSPITAL, INC.

The regular monthly staff meeting of the Bay State Hospital will be held on December 6 at the home of Dr. David J. Calicchio at 8:30 p.m. Dr. Harry Chaimson will discuss "Common Skin Diseases."

SPRINGFIELD ACADEMY OF MEDICINE

The next meeting of the Springfield Academy of Medicine will take place on December 11 at 8:30 p.m., at the Springfield Academy of Medicine, Spring and Frost Streets, Springfield.

Dr. Franz J. Ingelfinger will discuss "Diseases of the Pancreas."

SOCIETY MEETINGS AND CONFERENCES

NOVEMBER 30, DECEMBER 7, 14, 21 AND 28 AND JANUARY 4. New England Deaconess Hospital Clinic. Page 548, issue of October 4.

DECEMBER 1–22. The Springfield Hospital. Page 832, issue of November 22.

DECEMBER 2. American Academy of Dental Medicine. Page 548, issue of October 4.

DECEMBER 2 AND 3. American College of Chest Physicians. Page 752, issue of November 8.

DECEMBER 3, 6, 10 AND 13. Lowell Institute Lectures. Page 752, issue of November 8.

DECEMBER 4 AND 11. Boston City Hospital House Officers' Association. Page 832, issue of November 22.

DECEMBER 5–8. New York State Society of Anesthesiologists. Page 810, issue of November 1.

DECEMBER 6. Bay State Hospital. Notice above.

DECEMBER 8–13. American Academy of Dermatology and Syphilology. Page 752, issue of November 8.

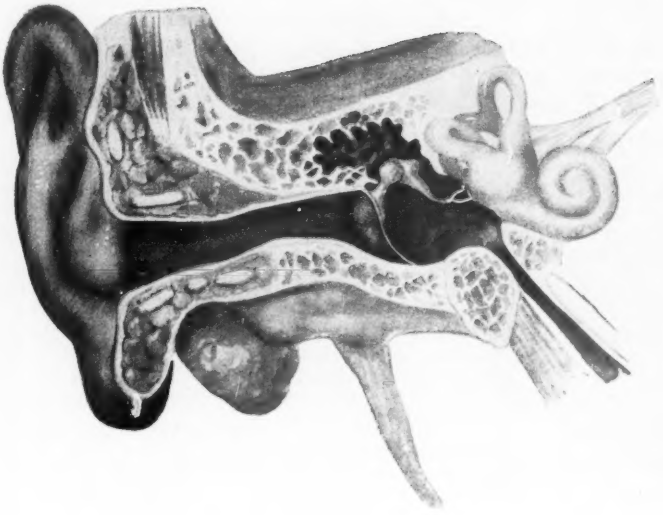
DECEMBER 11. Springfield Academy of Medicine. Notice above.

DECEMBER 11–19. International Congress on Mental Health. Page xiii, issue of July 26.

DECEMBER 12. New England Pediatric Society. Page 832, issue of November 22.

DECEMBER 13. Pediatric Problems of the General Practitioner. Dr. James Marvin Baty. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

(Notices concluded on page xiii)



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Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia General Hosp. 2:6 (Jan.) 1951.

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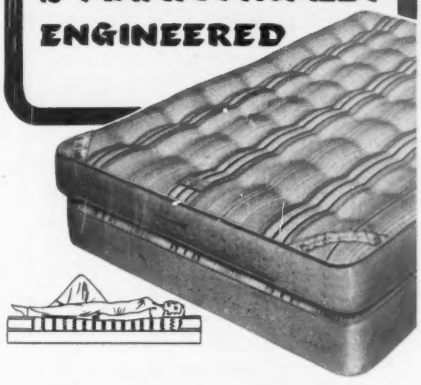

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NOTICES *(Concluded from page 874)*

DECEMBER 14 AND 15. Association for Research in Nervous and Mental Disease. Page 958, issue of June 21.

JANUARY 7, FEBRUARY 25 AND APRIL 15. Massachusetts Society for Research in Psychiatry. Page 792, issue of November 15.

JANUARY 9. Essex North District Medical Society. Page 832, issue of November 22.

JANUARY 22, FEBRUARY 26, MARCH 25 AND APRIL 24. Norfolk District Medical Society. Page 710, issue of November 1.

JANUARY 23. Suffolk District Medical Society. Page 669, issue of October 25.

MARCH 12. Northeastern New York Radiological Society. University Club, Albany, New York.

MARCH 31–APRIL 4. Fifth American Congress on Obstetrics and Gynecology. Page 832, issue of November 22.

MAY 1–3. American Goiter Association. St. Louis, Missouri.

JULY. Commonwealth and Empire Health and Tuberculosis Conference. Page 792, issue of November 15.

JULY 8–11. Thirteenth British Congress of Obstetrics and Gynaecology. Page xv, issue of December 14.

JULY 14–19. International Congress of Physical Medicine. Page 998, issue of June 28.

SEPTEMBER 7–9. Combined session of the New Hampshire and Vermont State Medical Societies, Mount Washington Hotel, Bretton Woods, New Hampshire.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 9. Pentucket Club, 111 Main Street, Haverhill.

HAMPSHIRE

JANUARY 2. Veterans Hospital, Northampton.
MARCH 5. Cooley-Dickinson Hospital, Northampton.
MAY 7. Annual Meeting. Jones Library, Amherst.

NORFOLK

JANUARY 22. Veterans Administration Hospital, West Roxbury.
FEBRUARY 26. Boston Medical Library.
MARCH 25. Boston Medical Library.
APRIL 22. Boston Medical Library.
MAY 7. Place to be announced.

SUFFOLK

JANUARY 23. Massachusetts General Hospital.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 6

THURSDAY, DECEMBER 6

*9:00–10:00 a.m. Cardiac Grand Rounds. Main Amphitheatre, Children's Medical Center.
9:00–10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
*12:00 m.–1:00 p.m. Guest speaker. Stearns Auditorium, New England Center Hospital.
5:00 p.m. Medical Education — A Concern of the People. Dr. James Howard Means. Boston Public Library.
8:30 p.m. Bay State Hospital Monthly Staff Meeting at the home of Dr. David J. Calicchio.

FRIDAY, DECEMBER 7

*8:15 a.m. Pregnancy. Drs. Story and White. Baker Clinic, New England Deaconess Hospital.
*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. New England Center Hospital.
*12:00 m.–1:00 p.m. Tumor Conference. Pratt Lecture Hall. New England Center Hospital.
*1:30 p.m. Tumor Clinic. Outpatient Department, Mount Auburn Hospital, Cambridge.

MONDAY, DECEMBER 10

*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street. Dr. Cleaveland Floyd in charge.
*12:00 m.–1:00 p.m. Hematology Conference, Stearns Auditorium. New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheatre, Peter Bent Brigham Hospital.
3:00 p.m. Gynecology Rounds. Mount Auburn Hospital, Cambridge.
5:00 p.m. Medical Education — A Concern of the People. Dr. James Howard Means. Boston Public Library.
*7:00–9:00 p.m. Combined Anesthesia Teaching Program of Boston. Stearns Auditorium, New England Center Hospital.

TUESDAY, DECEMBER 11

*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children. Massachusetts General Hospital.
*12:00 m.–1:30 p.m. Surgical Grand Rounds. New England Center Hospital.
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
7:00 p.m. Boston City Hospital House Officers' Association, New Cheever Amphitheatre, Dowling Building.

WEDNESDAY, DECEMBER 12

11:00 a.m. New England Pediatric Society. Medical Clinic. Main Amphitheatre, Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Medical Clinic (Children's Medical Center). Amphitheatre, Children's Hospital.
*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street.
*12:00 m.–1:00 p.m. Medical Conference. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Medical Center). Amphitheatre, Peter Bent Brigham Hospital.
12:30 p.m. Weekly Pathological Meeting. Joslin Amphitheatre, New England Deaconess Hospital.
*2:00–3:00 p.m. Combined Clinic of All Services (Children's Medical Center). Amphitheatre, Children's Hospital.
2:15 p.m. New England Pediatric Society. Scientific session. Amphitheatre C, Harvard Medical School.
*4:30–6:00 p.m. Physiology and Biochemistry Colloquium. New England Center Hospital.

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